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AN OUTBREAK OF TRICHINIASIS IN WOLVERHAMPTON AND DISTRICT

By J. H. Sheldon, M.D. Lond., F.R.C.P.

PHYSICIAN TO THE ROYAL HOSPITAL, WOLVERHAMPTON, AND THE GUEST HOSPITAL, DUDLEY; CONSULTING PHYSICIAN TO NEW CROSS HOSPITAL, WOLVERHAMPTON

At the beginning of this year five cases of a peculiar illness were seen at New Cross Hospital, Wolverhampton, in consultation with Dr. J. S. Lee, the medical superintendent, and a tentative diagnosis of acute trichiniasis was suggested.* This was based largely on the eosinophilia and muscle tenderness of certain of the patients, though other symptoms were hardly in accord with the textbook descriptions. At the same time three patients with obscure symptoms were admitted to the medical wards of the Royal Hospital, Wolverhampton, in whom the pathological department had demonstrated an eosinophilia. Inquiry among the practitioners of the district showed at once that since roughly the middle of December, 1940, a large number of patients had been seen with swollen eyes whose urine showed no evidence of nephritis. Through the coöperation of the practitioners, many of these have since been visited in their homes. Certain features of the disease, both clinical and epidemiological, which thereby came to light, appeared at first to make trichiniasis an unlikely diagnosis, and it seemed possible for a time that we were dealing with a new disease. At the suggestion of Dr. S. C. Dyke, Prof. W. W. C. Topley was approached, and after some of the cases had been seen by Prof. G. S. Wilson from the Emergency Public Health Laboratory, Oxford, Dr. Paul B. Beeson of Harvard was called in through the Ministry of Health. A discussion of the clinical problems with an American worker having first-hand experience of the disease was particularly helpful. On the day of his arrival, however, the diagnosis was established by Dr. J. S. Lee, when *Trichinella spiralis* was demonstrated in a biopsy of muscle from one of the cases at New Cross Hospital. It had only just entered the muscle, for there was no capsule formation. Next day Dr. S. C. Dyke found the trichinella in muscles removed from two of my patients at the Royal Hospital by Mr. R. Milnes Walker. Since then Dr. Lee has carried out a further successful biopsy at New Cross Hospital. The identity of the parasite has been confirmed by Prof. R. T. Leiper, who has, in addition, succeeded in obtaining embryos from the fæces of a patient now in the Royal Hospital. The diagnosis is thereby established.

CLINICAL COURSE

It is hoped to present a full description of the epidemic later, but in the meantime it seems essential to publish this short account, based on a survey of 76 cases. Trichiniasis has hitherto not been one of the ordinary gambits of clinical diagnosis in Great Britain. Further, the size of the outbreak here suggests that other places may well be affected, in which case there may be similar difficulties in diagnosis, for the clinical picture was by no means typical of the standard textbook description. The books describe three clinical stages corresponding to the life-history of the parasite—the invasion stage, characterised by gastro-intestinal symptoms such as vomiting and diarrhœa; the migration stage, characterised by fever, allergic phenomena (particularly swelling of the eyes), eosinophilia, and symptoms due to involvement of muscles, in which the diaphragm and larynx may be predominantly affected. The stage of encystment apparently produces no symptoms except cachexia in the severe cases. Osler states that "there may be" signs of central nervous involvement.

Early symptoms.—In this epidemic the first stage of gastro-intestinal symptoms was entirely absent, with very few exceptions.† In only 8 of the 76 cases (10%) was there early vomiting and in only 4 cases (5%) diarrhœa. The great majority of the patients complained of constipation from the start, and in some this was severe. Some had abdominal pain at the onset. Vomiting occurred in about a third of the cases in the middle of the illness, but this may have been due in part to the use of M. & B. 693. Some of the patients appear to have had coryza a week or more before the onset, but at this time of year colds are inevitably frequent. In a typical case the patient was in perfect health when he suddenly found his eyelids swelling, and as a rule he suffered at the same time from headache, sometimes severe. In many instances the swelling occurred while at work, but more often the patient went to bed and in the morning woke up very surprised to find that his eyelids were completely closed by swelling. The swelling was almost invariably bilateral, though occasional exceptions showed one-sided swelling; it was sometimes tremendous, with the conjunctiva protruding through the closed eyelids as a bulbous watery mass. In many cases there was hæmorrhage under the conjunctiva. The swelling varied in duration from 3 to about 10 days; usually it subsided considerably in 3 or 4 days and there was slight swelling for another 3 or 4 days. There was often associated œdema of the face, mainly in the cheeks and rarely in the lips, and in about a third of the cases patches of œdema appeared on the limbs or body. Rashes were very rare, but I twice saw an urticaria and once an eczema. The headache is usually frontal, often very severe, and may persist for a fortnight or more; in one case in the Royal Hospital it was relieved by a hypertonic enema.

Muscle involvement.—After about 3 days of swollen eyes and headache, during which most patients remained at work, pains appeared in the muscles, though these were sometimes absent. The presence of the parasite in a muscle does not necessarily cause pain, for in one of the biopsies trichinella was recovered in quantity from the vastus externus, yet the patient had never had any leg symptoms. The muscular pains ranged from a slight ache to a peculiar aching stiffness of such severity that the patients shuddered at the recollection, and three women told me that they would prefer to have labour pains. Stiffness may be a prominent feature, and in severe cases the patients have volunteered that they might just as well have been plaster statues. This appears to be most noticeable on initial muscular movement after rest, as in getting out of a chair or rising from bed. Several patients also volunteered the same story of a subjective feeling like "that of a leg which has gone to sleep before the pins and needles come." Weakness was a prominent symptom of many patients, and some were unable to lift the bedclothes for this reason. These muscular symptoms last from a day to 4 or 5 weeks. Stiffness of the neck was found in almost every case, and led in some instances to a diagnosis of meningitis, but this symptom is part of the general muscular affection. The stiffness is most obvious on attempts at lateral rotation of the head, rather than on back and fore movement. In addition to the neck, any or all parts of the four limbs has been the commonest localisation of the muscular symptoms, with pains in the back a frequent feature. There has been almost no affection of the diaphragm or laryngeal muscles, which is stressed in some accounts.

Eosinophilia was found in nearly every case, reaching a maximum of 51% but usually ranging from 25 to 45%. It was somewhat variable in its time incidence, and in the slighter instances might not appear till after the subsidence of symptoms. It was always present in the more severe cases, and in general its extent and persistence seemed to vary with the severity of the case.

Cough was present in about half the patients. It was usually an initial symptom appearing with the swollen eyes and headache. The cough was mostly dry for some

* A full account of these cases is given by Dr. Lee in the current issue of the *British Medical Journal*.

† More of the cases that are now appearing seem to have a short preliminary diarrhœa than did the early instances, and it is possible that the epidemic is changing its character in this respect.

days and then moderate sputum might appear. One patient had hæmoptysis as an initial symptom, and one a bronchopneumonia which went on to a clear pleural effusion.

The *urine* was reported as normal in almost all cases, and it was often examined since the œdema of the eyelids invariably raised suspicion of nephritis. Nevertheless, I have some doubt of the accuracy of these observations, for in several hospital cases albumin and blood were found in the urine for a short period—perhaps 24–48 hours—and thereafter the urine was normal. So many of the patients have stated that their urine was red for a day or so at the onset that an early and very temporary hæmaturia may in fact be frequent.

Except in subclinical cases the *temperature* was always raised and might be as high as 104° F. In an average case it rose to 101°–102° F. for a few days and then fell by a rapid lysis. In a few cases a temperature of about 102° F. persisted for as long as 3 weeks, and in these the whole clinical picture closely mimics typhoid fever. One such patient even had rose spots, but diagnostic features were the absence of splenic enlargement and the presence of cyanosis and extensor responses.

Central nervous involvement.—On these symptoms a clinical diagnosis of trichiniasis might reasonably be made, but a feature which caused difficulty has been the frequency of central nervous involvement. In the acute stage of some severe cases either of two clinical pictures might be suggested. The appearance was sometimes that of a coccal meningitis—the patient lying curled up in bed, with retracted head, photophobia and a piercing meningeal cry, semi-conscious and irritable, incontinent of urine and fæces, with a positive Kernig and extensor responses. The cerebrospinal fluid has, however, invariably been normal, and usually under normal or reduced pressure. The other picture was that of encephalitis, and one patient seen in consultation had the typical decubitus of encephalitis lethargica as I remember it from 1918, but without the ocular palsies; she subsequently developed cerebellar symptoms. The sleepiness of such a case is merely an advanced stage of a mental feature common to nearly all—a heavy sluggish lethargy in which for a time the patients are indifferent to their surroundings, and in particular resent any mental effort, such as answering questions. Another frequent mental state is depression of greater or less degree; in the most advanced example of this I was asked to see a patient who was said by the doctor to have "melancholia with a temperature," and after a complete clinical examination nothing could be added to his statement; it was only later that the true diagnosis was made. Temporary delusions have occurred in about 5% of cases, and the description by a mother that her daughter was "mithered and moaning" was accurate. No less than 13 cases (17%) have had clear evidence of focal damage to the brain. Among these, 5 had monoplegias and 4 had symptoms of unilateral damage to the cerebellum. To make matters more difficult, a few patients were found to have begun with this type of symptom. Thus, who would imagine that a boy who has a sudden attack of vomiting at school, and on being sent home has to clutch at surrounding objects to protect himself from a reeling giddiness, is suffering from the initial symptoms of trichiniasis? Who would anticipate that a woman who for 2 days had such weakness and giddiness that she could not even stand to dress herself would on the third day develop swollen eyes and thereafter the typical muscular pains? Or that a factory girl who for 3 days was so overcome with the desire to sleep that she was continually forced to go out into the open air would then develop swollen eyes and the remainder of the disease? These modes of onset are of course infrequent.

Hæmorrhage under the nails.—A further symptom which caused much interest and speculation was a peculiar type of hæmorrhage along the distal end of the nail bed of the fingers, following the curve of the nail. It was first noticed in 2 cases seen in private consultation, and a subsequent search in other cases showed that it was present in about 10%, and on the whole tended to be limited to the more severe types. Its presence was usually associated with much soreness in the tips of the fingers. At first red, it passed through plum colour to black and by that stage had become broken up into parallel lines running up under the nail for 4 or 5 mm. and looking as if a number of black splinters had got under the nail. In the initial stage its width was about 2 mm. and both edges were sharp. It was unlike anything met with before‡, and I have come to place considerable reliance on its diagnostic importance when present. It has never been observed in the feet, and for a time this gave rise to the speculation that some infecting parasite might be gaining entry into the body through the fingers. It occurred once as a prodromal symptom, and in the remainder at the height of the disease. It should certainly be looked for if cases occur elsewhere.

Subclinical cases.—In addition to the types of case outlined, examination of patients in their homes has revealed evidence of a considerable number of subclinical cases. The only symptom in such appears to have been a temporary swelling of the eyelids—of perhaps 2 or 3 days' duration but usually less—without constitutional symptoms of sufficient severity to cause the individual either to seek medical advice or to cease work. The percentages given earlier must therefore be taken as applying only to the type of case sufficiently serious to have sought medical aid, and not to the epidemic as a whole.

What to look for.—The only symptom common to every case seen is swelling of the eyelids; there has been considerable variation in both the presence and the relative time-incidence of the other features. To practitioners on the watch for trichiniasis it seems to be a sound rule, therefore, that unless nephritis is proved to be the cause, any patient with a history of swollen eyelids should be regarded as a possible case of trichiniasis, and further investigation, including an examination for eosinophilia, carried out.

EPIDEMIOLOGY

The extent of the epidemic is unknown. It has affected the whole of Wolverhampton, though not with an even distribution. There is evidence that cases are occurring to the south and to the east of the town. The number of people affected is also unknown, but two independent lines of evidence—neither of which is strong—agree to suggest that probably not less than 500 cases have sought medical attention; this is probably an underestimate and takes no account of subclinical cases. The epidemic seems to have begun with a few cases during the second week of December, 1940. There was a great rise in incidence about Dec. 18, and cases seem to have occurred at this level until the end of the first week in January. Since then the incidence seems to have decreased, but numerous fresh cases are still arising. An unusual but very fortunate feature for an epidemic of this size is that so far as can be ascertained there has been no death. This is of greater interest in that Osler states that "early diarrhœa and moderately intense gastro-intestinal symptoms are, as a rule, more favourable than constipation." In the present epidemic preliminary gastro-intestinal symptoms have been mainly absent, and constipation frequent.

There has been a definite social incidence. Broadly speaking, the disease has been limited to industrial workers, and the great bulk of cases has been visited in the new housing estates and similar types of home in the older parts of the town. At an early stage of the inquiry it became evident that there was a definite sex-incidence. A high proportion of the patients were adult women. Though more male cases have since been met with, this statement remains true, for of the 76 cases already seen, 14 are male and 62 female. There is therefore a rather more than four to one feminine preponderance. Only 2 are children, and this small incidence is probably due to their small consumption of pork; this is supported by the impression that many of the subclinical cases have been in children. The female incidence threw an undue strain on the imagination until the reason was discovered, and for a time it seemed possible that the disease might be due to some new factor in feminine life imposed by war conditions.

The explanation both of the sex and the social incidence was discovered by a lucky accident. With the

‡ Dr. Paul B. Beeson has informed me that this nail sign was first described by Dr. J. B. McNaught in 1939 (*Amer. J. trop. Med.* 1939, **19**, 181) in an article on the diagnosis of trichiniasis. I have not seen the original, but it apparently confirms the emphasis laid on the diagnostic value of the sign.

possibility of trichiniasis in mind, inquiries of patients were still being directed to their pork consumption. At one house the daughter, after denying pork pie, was asked about sausage, when before she could get a word out, her mother burst forth in righteous indignation with "Now then, I've told you never to eat 'em raw"! As that—though quite unexpected—seemed a promising line of inquiry, it was followed up, and, to my great astonishment, of the next 59 patients no less than 37 confessed to the habitual practice of eating raw uncooked pork sausage. This helps to explain both the huge size of the epidemic and its social incidence, and is incidentally a magnificent testimonial to the efficiency of the meat inspection in the past. In itself it offers no explanation of the sex-incidence. As it seemed important to discover the incidence of "raw sausagers" in the general population, three practitioners with patients among the social class concerned kindly undertook to ascertain the frequency of the habit from a consecutive series of patients attending their surgeries who were unaffected by the present disease. In one inquiry 50 patients were asked whether raw sausage was eaten in their household; 27 answered yes and 23 no. In the other two inquiries, the people were asked whether they actually ate raw sausage themselves, and of 74 only 23 answered yes and 51 no. These inquiries suggest that raw sausage is eaten in at least half the working-class households of the district, but not by everyone in the household. It is in the last factor that the peculiar female incidence of the disease finds its explanation, for of the 23 unaffected people with the habit of eating raw sausage only 3 were men while 20 were women. Thus the size, social and sex-incidence of the epidemic receive an approximate explanation.

The reasons for the greater incidence of "raw sausagers" in women are interesting.

It was clear from the answers of the patients that, while some definitely considered sausage more tasty raw than cooked, many of the factory girls were attached to raw pork sausage spread on bread as a tasty and portable lunch to take to work, or liked it when they came home as easy to prepare. The men on the other hand felt they had earned a cooked meal. Many of the patients were married women, and their usual reason was different. During the morning they had got their husband his breakfast, packed the children off to school, washed up the breakfast things, tidied the house, made the beds, and done the shopping with no chance of rest or refreshment. By the time it came to prepare the midday meal the smell of the frying pan was altogether too much, and they eased their hunger by nibbling half or more of a raw sausage while the rest were frying. It would be interesting to know whether eating raw pork sausage is a general habit of the English industrial workers or only a Staffordshire peculiarity. If trichiniasis does appear elsewhere it is clearly of the first importance to direct early attention to this question. Here the medical officer of health at once issued a public warning in the local press.

SUMMARY

An epidemic of trichiniasis has appeared in Wolverhampton and district during the last five weeks, which appears to have affected at least 500 people. It is still active. There have been no deaths.

There have been almost no preliminary gastro-intestinal symptoms. In addition to muscular pain, stiffness and weakness, a fairly large proportion of cases have had focal signs of central-nervous trouble as well as temporary mental changes. All the cases have had swelling of the eyelids, which is the single symptom common to all, and if other outbreaks are similar, doctors should pay great attention to this feature.

An additional sign which when present has been of diagnostic value is a line of hæmorrhage along the distal margin of the nail-bed of the fingers. Epidemiologically, the disease has been confined to the industrial working-class with a heavy incidence in the female, both of which features appear to be due to the relative incidence of the habit of eating uncooked pork sausage.

I must express my thanks to Dr. J. S. Lee for the opportunity of seeing the initial cases, and for his coöperation since; to Dr. S. C. Dyke and the staff of the pathological

Continued at foot of next column

A NEW CONCEPT OF THE TOXÆMIA OF DIPHTHERIA

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IT has long been recognised that diphtheria has exhibited a much greater severity in certain areas than in others, but, following an early controversy, it was usually accepted until quite recently that diphtheria antitoxin was an effective remedy for use in treatment of the disease. That antitoxin has saved many lives no unbiased observer will question, but it has proved much less effective in combating the toxæmia of diphtheria than was to be expected from the promising results obtained in the early days of its use. Where, after a lapse of years, severe diphtheria revisited areas in which the fatality-rate was formerly high but had fallen since the introduction of antitoxin serum was found to be relatively ineffective to cope with the altered conditions. Thus Deicher and Agulnik (1927) recorded a steady rise in the fatality-rate from diphtheria in the Virchow Krankenhaus from 5% in 1924 to 26·7% in the first five months of 1927. Similar experiences were later recorded from other parts of Europe and a noteworthy feature was the occurrence of toxæmic diphtheria of the severest type in older children and even adults.

To appreciate to the full how antitoxin failed in the changed circumstances, it must be recalled that in the interval between its introduction and the time when certain heretics began to feel that something was amiss all sorts of technical improvements in its production had taken place. It contained a larger number of standard units in a given volume than ever before and the dosage readily available for treatment was, in consequence, on a more liberal scale than had previously been possible.

The darkness was illuminated when Anderson, Happold, McLeod and Thomson (1931) of Leeds published their work showing that diphtheria bacilli could be divided on morphological appearances and cultural characteristics into three types called gravis, mitis and intermedius. They were able to correlate the occurrence of severe types of diphtheria in certain areas with the prevalence in those areas of the gravis type of organism. The literature which has since appeared on the subject makes it clear that the gravis and intermedius types cause diphtheria in which toxæmia is a predominant feature and the fatality-rate and incidence of toxic complications is correspondingly high, whereas, with few exceptions, mitis strains cause a diphtheria in which the incidence of toxæmia is low and fatalities, when they do occur, are not usually due to toxæmia but to the mechanical effects of the spread of membrane to the larynx and lower air-passages. In Dublin the gravis type of organism is very prevalent and can be isolated from about 85% of all cases admitted to Cork Street Fever Hospital. Admissions include a large number of hypertoxic cases of diphtheria every year, among whom the fatality-rate is very high despite maximal doses of the antitoxin now issued by the commercial houses for general use being administered without delay.

This discrepancy between the alleged effectiveness of diphtheria antitoxin—one may say its proved effectiveness in laboratory tests—and its comparative or total failure in the treatment of severe toxic diphtheria has

Continued from previous column

laboratory of the Royal Hospital, Wolverhampton, for their help with the pathological studies; and to Drs. W. Bentley, E. P. Drabble, C. A. Day, A. W. Lloyd-Davies, J. F. Lyne, J. N. McTurk, A. D. Millington, S. Robinson, A. V. Russell, W. R. Somerset and W. Wallace for their help both in allowing me to visit their patients and in the provision of much general information.

not hitherto been capable of explanation. All investigators have agreed that gravis, intermedius and mitis strains of bacilli produce the same toxin neutralisable by the antitoxin in common use, which is prepared by immunising horses with toxin obtained from cultures of the Park-Williams No. 8 strain. Yet there is reason to believe that when antitoxin was first introduced it was a most valuable specific, even in quite small doses, for the treatment of very severe toxic cases. Using doses of probably not more than 8500 units in any case, Roux, Martin and Chaillou (1894), who were dealing with severe diphtheria showing well-marked toxic manifestations, recorded very satisfactory clinical results and a striking reduction in mortality.

These results, which I have discussed in some detail elsewhere (1939), were not unique, for Ehrlich, Kossel and Wassermann (1894) had already had virtually the same experience with exceedingly small doses of antitoxin in Berlin, where diphtheria was also very severe at the time, but they present a striking contrast to those now obtainable even with enormous doses of modern antitoxin. Taking into consideration also the testimony of the older clinicians now living who had personal experience of the positive effects of diphtheria antitoxin when first introduced on the toxæmia of the disease, there can be no reasonable doubt that in the interval between the first clinical use of diphtheria antitoxin and the present day some factor has been missed. This probability is rendered the greater by the fact that the development of antitoxin has been dictated not by increased clinical efficacy but solely by the desire to increase the unitage per unit volume as determined in the laboratory. The successive stages by which modern antitoxin has evolved from its precursor, the universal introduction of the Park-Williams No. 8 strain for the preparation of toxin used in immunisation, the substitution of Römer's and Ramon's methods of testing for Ehrlich's, the concentration of antitoxin by ammonium-sulphate precipitation and finally its refinement by digestion, all hailed as scientific triumphs, have never received other than the most superficial clinical tests for their influence on therapeutic value. They are of importance primarily because they assist manufacturers to comply with the Therapeutic Substances Regulations, which impose a minimum standard unitage (400 units per c.cm.) on any serum which may be sold, irrespective of its therapeutic qualities, and to satisfy the contract requirements as to unitage of local authorities.

WHY MODERN ANTITOXIN FAILS

It is now possible, however, to suggest a reason why modern antitoxin fails to cope with diphtheritic intoxication, based on a new concept of the nature of the toxæmia encountered in severe toxic diphtheria. There had been no condition experienced by laboratory workers in guineapigs which resembled clinical hypertoxic diphtheria until I was able to demonstrate (1940) that it could be reproduced by a combination of saline extracts of gravis strains grown on solid media with doses of Park-Williams No. 8 toxin less than the minimum lethal dose.

The classical diphtheria toxin derived from the Park-Williams No. 8 strain produces in the guineapig a disease which bears but slight resemblance to the hypertoxic human case. In doses just sufficient to kill, the animal dies in a few days with a local lesion consisting of slight œdema, necrosis and congestion, and usually shows post-mortem definite congestion of the suprarenal glands, pleural effusion and congestion of the intestines. If the dose of toxin be increased the animal dies more rapidly but the post-mortem findings are not an exaggeration of those already mentioned; on the contrary, they are often almost entirely negative. Furthermore, it has long been known that fresh toxins as prepared in the laboratory have little tendency to cause postdiphtheritic paralysis when inoculated in non-lethal doses, although old laboratory toxins which have deteriorated may do so.

It was found, on the other hand, that by growing gravis strains on Loeffler's serum and suspending the growths in saline, from which the organisms were subsequently removed by centrifuging or filtration, preparations were obtained which had distinctive properties, more especially on intradermal inoculation into guineapigs, and did not conform to ordinary diphtheria toxin prepared in the laboratory. One of their most striking characteristics was their tendency to cause a lesion which was progressive from the time of inoculation, unlike Park-Williams No. 8 toxin which requires a latent period of many hours before any reaction can be detected no matter in what concentration it may be employed. This was obviously more in accord with the fulminating local lesion of hypertoxic diphtheria in which an extensive inflammation may be apparent where a few hours previously little or nothing was visible. On the other hand, it was not possible by subcutaneous inoculation of these preparations into guineapigs to produce the appearance of hypertoxic diphtheria; they were of definite but low toxicity for guineapigs. When, however, the preparations made from the gravis strains were combined in suitable doses with toxin prepared from the Park-Williams No. 8 strain the picture of hypertoxic diphtheria as it occurs in the human being could be faithfully reproduced in guineapigs.

The conclusion seemed, therefore, inescapable that in the causation of hypertoxic diphtheria two substances, which we may provisionally call substance A and substance B, are necessary, and that these are both produced by the diphtheria bacillus in the body of the victim. Moreover, diphtheria toxin in general is composed of the two substances and the effects which it produces in human disease or in the experimental animal are governed by the total amounts and relative proportions in which they gain admittance to the tissues of man or animals. The fraction of toxin which is of high lethal value for the guineapig and predominates in Park-Williams No. 8 toxin as usually prepared is substance A, and that which predominates in the saline extracts made from growths of gravis strains on Loeffler's medium and in diphtheria toxin as produced in the body in hypertoxic cases is substance B. In simple form:

Diphtheria toxin	= substance A + substance B
Park-Williams No. 8 toxin	= high proportion of substance A + substance B
Toxin produced in hypertoxic diphtheria	= high proportion of substance B + substance A

The effect of the substance-B component of toxin is to promote the penetration of the tissues by substance A, thus enabling it to cause its specific damage, and when present in excess it leads to a great increase in the size of the local lesion, in the gelatinous œdema which accompanies it, in the amount of necrosis produced and in the tendency for wasting and paralysis to set in later. It has little or no influence on the minimum lethal dose of toxin as that unit has been defined by immunologists, since by definition death of the experimental animal must take place within five days. Later deaths, which are frequent when quantities of the classical toxin less than the minimum lethal dose are injected in combination with substance B, and which show many points of similarity with what is found in severe clinical diphtheria, are not considered.

The clinical toxæmia with which diphtheria is associated may therefore be interpreted rationally in terms of laboratory findings. The gap has been bridged between the clinical finding that the diphtheria bacillus, which is capable of causing an overwhelming toxæmia in patients, can, in the laboratory, produce only insignificant amounts of toxin as judged by the usual tests and the laboratory finding that strains clinically insignificant are often the best toxin-producers. The production and testing of diphtheria toxin in the laboratory has been biased by the more obvious effects of substance A in the guineapig and test-tube, and, since the activities of substance B have either not obtruded themselves or have been incapable of rational explanation when they did, they have been relegated to a position of minor importance.

We must next consider how these findings influence the all-important behaviour of antitoxin in neutralising toxin and more especially in relation to its use in the treatment of diphtheria. In the first place, it is to be expected that in diphtheria antitoxin are to be found two antibodies corresponding to the two constituents of toxin, and it must necessarily follow that, with any given toxin and antitoxin, a perfectly exact fit, so that both constituents of toxin are equally neutralised at the end point in a neutralisation test, must be exceedingly rare. There must always be at the end point in such tests an

excess of one or other of the neutralising antibodies. In this fact we find a feasible explanation of Ehrlich's phenomenon that more than one minimum lethal dose of toxin has to be added to the Lo dose—that is, the dose of toxin which in combination with one unit of antitoxin causes no symptoms when inoculated into an animal, in order than the L+ dose, or dose which in combination with one unit of antitoxin causes death of the animal within the standard period of five days, may be obtained.

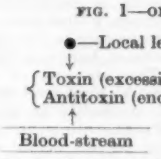
AVIDITY OF ANTITOXIN

From a knowledge of the existence of the two substances in toxin and antitoxin and of their behaviour it is possible to explain why ordinary antitoxin fails to cope with the toxæmia accompanying gravis infections in hypertoxic cases of diphtheria. About thirty years ago a controversy, which has since been almost forgotten, raged around the question of the efficacy of antitoxin. It was held among others by Kraus and his associates (Kraus and Baecher 1913) that antitoxin owed its therapeutic efficiency to an ill-defined property known as avidity instead of to its unitage, as was more generally believed. More recently avidity has come in for special study and the term is now used in two senses: that of rapidity of combination with toxin (Madsen and Schmidt 1926) and of firmness of combination with toxin (Glenny and Barr 1932). It seems probable that the different points of view as to the meaning of the term are related to questions of degree rather than of fundamental nature. If, however, we consider avidity in the English sense as firmness of combination certain important results follow from the fact that diphtheria toxin is composed of two substances and antitoxin of two others.

The cardinal distinction between avid and non-avid antitoxins is that avid antitoxins still remain firmly united to toxin when neutral mixtures of the two are diluted, whereas non-avid antitoxins dissociate from combination with toxin in similar circumstances so that a mixture which is apparently neutral when inoculated into an animal in concentrated form shows toxic properties if diluted a hundred times before inoculation. Similarly, a small dose of a neutral mixture of toxin and non-avid antitoxin possesses toxic properties if inoculated into a test animal because of the dilution which takes place in the body of the animal, whereas a large dose of a similar neutral mixture may show no toxic effects. Intimately bound up with the question of avidity is the so-called Danysz phenomenon which was shown by von Dungern (1904) to apply to diphtheria toxin and antitoxin. If to a unit of antitoxin a unit of toxin be added a neutral mixture is obtained, but if to a unit of antitoxin a fraction of a unit of toxin be added and the mixture be allowed to stand for a time, the antitoxin is no longer capable of neutralising the remainder of a unit of toxin supplied in a second addition. It has been possible to show that the toxicity of the mixture following the second addition is in the main due to the fact that the antitoxin has been rendered non-avid by the first addition. The antitoxin is no longer capable of binding toxin firmly but, on dilution, dissociates from it.

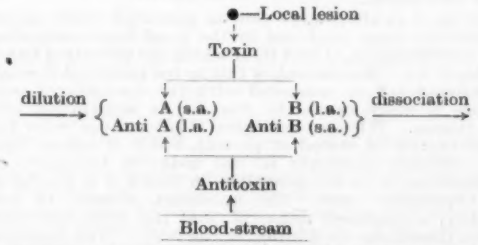
This has a most important bearing on the therapeutic use of antitoxin. When antitoxin is administered to a case of diphtheria and after administration circulates in the blood it is met by a stream of toxin entering from the site of its production in the diphtheritic lesion. After combination of the antitoxin with toxin the mixture is diluted in the blood-stream. If the antitoxin be non-avid, dissociation will take place and the toxin will still be able to exert its toxic effects though possibly in modified form. It is even conceivable that in certain instances such antitoxin will accelerate the death of the patient by accelerating the distribution of toxin, the non-avid antitoxin acting as vector. But even should the antitoxin used for treatment possess ordinary avidity it will tend to become non-avid as a result of the additions to it of toxin derived from the local lesion. This is the more likely to occur in hypertoxic cases where substance B is being produced in excess in the local lesion. In the first place, antitoxin reaching the local lesion has insufficient antibody to substance B to enable it to neutralise this component of toxin. Substance A will be neutralised locally, only to be dissociated once more from its combination with antitoxin on dilution

FIG. 1—OLD CONCEPT



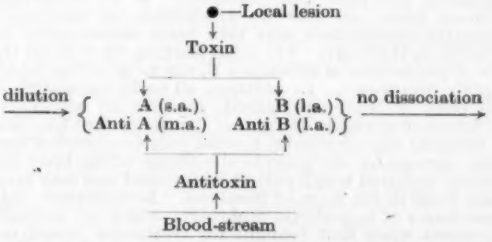
Result: Neutralisation of toxin (in theory only).

FIG. 2—NEW CONCEPT



Result: B not neutralised. Antitoxin rendered non-avid. No true neutralisation of toxin. Local lesion persists. Toxæmia persists.

FIG. 3—AVID ANTITOXIN



Result: B neutralised. Firm union of toxin components with antitoxin components. Local lesion eradicated. Toxæmia halted, leaving only that due to absorption of toxin prior to administration of antitoxin.

s.a., l.a., and m.a. = small, large, and moderate amounts.

in the body. Modification of the local lesion will, therefore, take place, but not its abolition. The local lesion will persist, toxin absorption will continue and general toxæmia due to the dissemination of toxin to the vital organs throughout the body will pursue a modified, though none the less irresistible, course. Clearly, antitoxin treatment of hypertoxic cases of diphtheria can only meet with success when such antitoxin is available as will neutralise without delay in the local lesion the all-important substance B and by its eradication halt the toxic onslaught, which will likewise and by the same fundamental mechanism ensure that a firm union between toxin and antitoxin takes place so that no dissociation can follow dilution of the mixture in the circulation after absorption, and which will, finally, be able to withstand the addition to it of quantities of toxin rich in substance B without forfeiting its avidity. None but the most avid antitoxins would be capable of fulfilling these requirements, whereas the antitoxins in general use today are of low avidity.

TOXIN-ANTITOXIN ACTION

A picture of what was formerly believed to occur in cases of hypertoxic diphtheria contrasted with what in all probability does occur, and its bearing on the use of antitoxin is provided by the diagrams. Fig. 1 shows the concept of hypertoxic diphtheria hitherto held—that in these cases a superabundance of a single entity diphtheria toxin is produced in the local lesion and can only be countered by antitoxin of ever increasing unitage administered in progressively greater doses. It is based on a false analogy. It is assumed that hypertoxic

diphtheria in the human being is equivalent to the administration of many minimum lethal doses of Park-Williams No. 8 toxin to the guineapig in the laboratory. There is in reality no comparison between the two, as has already been shown. The amount of guineapig acute killing factor (substance A) produced in the local lesion of a hypertoxic case is probably at most only a few guineapig lethal doses. Furthermore, in hypertoxic diphtheria most of the deaths do not occur within the first few days, as they would if they were due to overwhelming doses of an acutely lethal toxin, but are due to cardiac failure which sets in about ten days after admission to hospital.

In fig. 2 an alternative view is presented which shows diphtheria toxin produced in the local lesion consisting of two substances, A and B, of which the guineapig lethal factor is A. The amount of this factor produced is small—insignificant as compared with the quantity of substance B which opens the way for its penetration into the tissues. Whether substance B is toxic per se for the child cannot be stated at present, but it is certain that the ordinary antitoxin in use today is incapable of neutralising it in the quantities in which it is produced in hypertoxic cases. The antitoxin, already of low avidity, is rendered non-avid, and the toxin-antitoxin union dissociates on dilution in the body. The toxæmia of the disease continues almost unabated.

Fig. 3 shows diagrammatically what happens when a truly avid antitoxin, able to neutralise substance B, is employed for the treatment of a hypertoxic case. Relatively small doses of the antibody to substance A are adequate provided that substance B is neutralised without delay, so that no dissociation of the toxin-antitoxin combination may take place subsequently on dilution in the body. The most striking effect is on the site of production of substance B, the local lesion, which rapidly disappears. In addition, all toxin circulating in the body is truly neutralised, so that all immediate evidences of toxæmia disappear. If the patient has been ill for some days, however, it must only be expected that some damage by the toxin to the tissues of the body has already occurred which cannot be reversed and may later show itself in the form of paralysis. Nevertheless, only those cases of hypertoxic diphtheria which are actually moribund when first brought for treatment should die if an antitoxin of proper quality were available for their treatment.

I have already noted (1940) that the second component of diphtheria toxin, substance B, which is of greatest importance in the causation of clinical toxæmia, has properties in many respects similar to those of the diffusion factor of Duran-Reynals (1933) and McClean (1936). Evidence of their identity is accumulating which I hope soon to be able to publish. Diffusion factors or mucolytic agents, as they are called, following the work of Chain and Duthie (1939), are shown to be very widely distributed according to the recent review of the subject by Favilli, McClean and Hale (1940). The probability, therefore, increases that it will be possible in the future to produce effective antitoxins for the treatment of many types of toxæmia in addition to diphtheria.

SUMMARY

Comparison between the clinical results obtainable with diphtheria antitoxin when first introduced and that now in general use shows that in the development of antitoxin some essential factor has been missed.

A new concept of the nature of the toxæmia of diphtheria and of the specific treatment required to combat it successfully is advanced, based on the following considerations. Diphtheria toxin is composed of two substances, one of which (substance A) is highly lethal for the guineapig and is present in large amounts in Park-Williams No. 8 toxin as prepared in the laboratory. Little of this constituent is produced in the body of the victim of diphtheria although it has hitherto been assumed that hypertoxic diphtheria is caused by its production in excessive amounts. Conversely, laboratory toxin contains relatively little of the second constituent (substance B) but it is this substance, produced in excessive amounts, which determines the occurrence of hypertoxic cases of diphtheria. The effects of substance B are to promote the penetration of the tissues by substance A, and when present in excess it leads to a great increase in the size of the local lesion, in the gelatinous œdema which accompanies it, in the amount of necrosis produced and in the tendency for wasting and paralysis later. Corresponding to the two substances in toxin there are two antibodies in antitoxin. Ordinary antitoxin contains a high proportion of the antibody to substance A but is deficient in antibody to substance B. When this type of antitoxin is used in the treatment of hypertoxic cases of diphtheria, substance B is not neutralised and the antitoxin is rendered non-avid. Dissociation of toxin from its combination with antitoxin therefore takes place on dilution in the body and the toxæmia continues almost unabated. The avidity of antitoxin is determined by its power of neutralising substance B, and for the treatment of the toxæmia of diphtheria antitoxins rich in the antibody to substance B are required.

I am indebted to the Medical Research Council of Ireland for their assistance which enabled me to pursue the investigations recorded in this paper.

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TREATMENT OF HYPERTOXIC DIPHTHERIA WITH AVID SERUM

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MEDICAL SUPERINTENDENT OF CORK STREET FEVER HOSPITAL, DUBLIN

A VARIETY of hypertoxic diphtheria has been extremely prevalent in Dublin in recent years. One of its outstanding features is the faucial œdema which accompanies the deposition of membrane on the tonsils and structures of the faucial ring. This is so striking in some cases that it has been mistaken for quinsy, and at least one of the cases here reported was subjected to incision before admission to Cork Street. Associated with the faucial œdema is a rapidly developing cervical cellulitis, a diffuse cellular infiltration involving the whole of the tissues, including the glands, of the sides and front of the neck, extending for 2–3 in. below the lower jaw. This "bull neck" is invariably present in hypertoxic diphtheria and subsides without suppuration pari passu with the clearing of the diphtheritic membrane and the disappearance of faucial œdema. A certain proportion of cases exhibit hæmorrhages into the skin and subcutaneous tissues as well as from mucous membranes; such cases are the most serious of all and are represented as being invariably fatal in standard textbooks. The appearance of albumin in the urine after the fourth day of disease is another constant feature in hypertoxic diphtheria. It seems to be related to the elimination of unneutralised toxin by the kidney, and may persist for 10–14 days or even longer after the patient comes under treatment. Fall in blood-pressure is another constant manifestation; the fall is generally greatest immediately prior to the development of signs and symptoms of cardiovascular failure. Cardiovascular failure is, of course, the cause of death in the fatal cases. As a rule it shows itself in the second week of the disease—most usually 7–10 days after admission. The more toxic the case the earlier the symptoms of cardiovascular failure. Some cases, overwhelmed by toxæmia, show cardiovascular failure as early as the fifth or sixth day.

CLASSIFICATION OF CASES

For purposes of comparison we classify our cases in Cork Street into four grades.

Grade 1.—Membrane taking the form of "speckling" or "spotting" or "scattered patching," confined to the tonsils. Pure laryngeal cases are included. If death occurs it is due to some intercurrent cause, not to diphtheria toxæmia.

Grade 2.—Coherent patch of membrane confined to the tonsils or its pillars, but not involving the palate. Toxæmia present and paralytic sequelæ (e.g., palatal or ciliary) not unusual. Laryngeal cases with faucial lesions not extending over the pillars are included. If death occurs, it is due to the same cause as in grade 1.

Provided there is no faucial œdema and, of course, no bull neck no case in grades 1 or 2 should die of toxæmia if given ordinary commercial antitoxin with reasonable promptitude. With the remaining two grades the story is very different. For some reason the prognosis in diphtheria is radically altered once the membrane extends on to the soft palate. This is not merely a question of amount of membrane—large tonsils may accommodate more membrane than small—but if the membrane on shrunken tonsils crosses the anterior faucial pillar and invades the palate dangerous cardiovascular sequelæ are to be expected. The severity of the case is proportional to the extent of this palatal invasion.

TABLE I—CLINICAL FEATURES IN DIFFERENT GRADES OF DIPHTHERIA

—	Grades 1 and 2	Grade 3	Grade 4
Bull neck ..	—	+ +	+ + +
Faucial œdema	—	+ + or +	+ + + or + +
Membrane— on palate ..	—	+ +	+ + or +
on uvula ..	—	+ or −	+ or −
Nasal discharge	—	+ or −	+ or −
Albuminuria ..	—	+ + or −	+ + or +
Cardiovascular failure ..	—	+ + or + or −	+ + or + + +
Paralyses ..	Grade 1 − Grade 2 + (often single)	+ + or + (if survive often multiple)	+ + (if survive often multiple)
Hæmorrhages	—	—	+ +
Case-fatality rate*	Less than 1%	About 25%	100%

* Textbook figures.

If it extends to the base of the uvula it generally meets membrane advancing from the other side, and investment of the uvula wholly or in part may take place. Spread of the membrane over the posterior pillar, which goes on simultaneously, leads ultimately to the invasion of the nasal cavities from the back, and this membrane proceeds to cover the turbinates and septum, but, being partially liquefied by the tears and nasal secretions, first manifests itself in the form of profuse purulent nasal discharge.

Grade 3.—Membrane involving the palate, with or without investment of the uvula and nasal discharge. Usually with much faucial œdema, bull neck and, if the patient survives long enough, multiple paralyses. Toxæmia considerable. These cases, by reason of their frequency, constitute the main part—fully 75%—of the gravis diphtheria problem.

Grade 4.—Cases with toxic hæmorrhages from mucous membranes and into subcutaneous tissues with bruising at the site of injections, associated with diphtheritic lesions in the nasopharynx, including much œdema in the throat. Toxæmia extreme. Cardiovascular failure inevitable when treated with commercial antitoxins. In those who survive, multiple paralyses almost invariable. These cases constitute the remaining 25% of the gravis diphtheria problem.

The clinical features of the different grades are contrasted in table I. These grades represent different stages of one process—the circumferential spread of diphtheritic membrane. This faculty of circumferential spread, by which discrete speckles, spots and patches of diphtheria membrane coalesce and become one coherent patch, which, then invades the extratonsillar tissues, has been long recognised, but up to now sufficient stress has not been laid on the time factor. In the classical diphtheria of the textbooks membrane spreads in a leisurely way during the first four days of the disease, but in hypertoxic diphtheria membrane, in the form of small patches confined to the tonsils, can become an extensive investment of the whole of the structures of the faucial ring within 24–36 hours, and this rapid spread is accompanied by severe faucial œdema. The summation of extent of membrane, plus faucial œdema, accurately indicates the degree of toxæmia and gives a measure of the severity of the case. In one patient there will be a great deal of membrane, covering the tonsils, palate and uvula completely, and accompanied by nasopharyngeal involvement, but relatively little œdema, and in another there will be a moderate amount of membrane covering tonsils and part of the palate with enormous faucial œdema. These are grade-3 cases and all have bull necks. The worst are those where membrane and faucial œdema are accompanied by hæmorrhages from mucous membranes and into the skin and subcutaneous tissues. These are the grade-4 cases.

TABLE II—RESULTS IN CASES OF DIPHTHERIA TREATED WITH COMMERCIAL ANTITOXIN IN 1939 AND 1940 (11 MONTHS)

—	Cases	Deaths	Case-fatality rate %
Grade 1.. ..	564	3	0·53
„ 2.. ..	262	3	1·14
„ 3.. ..	188	30	15·95
„ 4.. ..	71	33	46·48
Totals	1085	69	6·36

In Cork Street among grades 1 and 2 we have a case-fatality rate of 1% or less (mostly attributable to pulmonary diphtheria or intercurrent infections), but in grade 3 it is from 15 to 20% and in grade 4 not far short of 50%. In the fifteen months prior to the arrival of the new avid serum 259 cases of grades 3 and 4 were admitted to the wards. Of these 63 died, a case-fatality rate of 24·3%. If the grade-4 cases alone are considered (71 with 33 deaths), the rate is 46·5% (see tables II and III). All of these 259 patients received maximal doses of commercial antitoxin—i.e., 120,000 units, mostly given in the form of an initial intramuscular dose of 60,000 units followed by an intravenous dose of 60,000 units six hours later.

TABLE III—RESULTS IN CASES OF DIPHTHERIA OF GRADES 3 AND 4 TREATED (1) WITH COMMERCIAL ANTITOXIN, (2) WITH AVID SERUM AND (3) WITH SERUM OBTAINED FROM THE SAME HORSE AT A LATER STAGE OF IMMUNISATION

—	Cases	Grade 3	Grade 4	Deaths	Case-fatality rate %
Commercial antitoxin (all maximal doses)	259*	188	71	63	24·3
Avid serum (maximal doses to 4 only) ..	16†	8	8	1	6·2
Control serum (all maximal doses) ..	20*	9	11	8	40·0

* Unselected, consecutive. † Selected for their exceptional severity.

RESULTS WITH AVID SERUM

When Dr. R. A. Q. O'Meara came to Dublin I put before him the problem of these grade-3 and 4 cases. Dr. W. J. Roche, my assistant, furnished him with swabs, cultures, pieces of membrane, post-mortem tissues and samples of blood taken at different stages of the disease. In April, 1940, a small quantity of avid serum, supplied by the Wellcome Physiological Research Laboratories, was sent to Cork Street Hospital. It is impossible to express avidity numerically because no suitable standards for its laboratory assay are yet available, but this serum was notably more avid than commercial antitoxin.

This avid serum was not produced by any special methods of immunisation of horses. It was discovered at the Wellcome Laboratories that this particular serum contained an abundance of the "anti-B" factor which Dr. O'Meara believes to be essential in the treatment of

hypertoxic diphtheria, and that commercial antitoxin contains this factor to a much less extent. The amount of serum available was limited by the fact that it has not yet been possible to produce the serum at will, although efforts are being made with this end in view. We decided to use it only on the most severe grade-3 or grade-4 cases admitted. We had enough to treat only 16 of these specially severe hypertoxic cases; actually 8 were grade 3 and 8 grade 4. For the first 4 cases we adhered to the maximal dosage we had been accustomed to give of commercial antitoxin. But as the results obtained were much better than those with commercial sera, and as we wished to treat as large a series as possible with the small quantity of the new serum available, we decided to risk giving much lower doses to the remaining 12 cases. Among these 16 hypertoxic cases of diphtheria, specially selected because of their exceptional severity, only one died, a grade 4, which received 24,000 units of avid serum.

The case-fatality rate of 6·2% is only a quarter of that prevailing in the much larger series treated with commercial antitoxin in spite of two considerations that heavily weighted the scales against the new serum—(1) that the cases given the new serum were all selected because of their extreme toxicity, as being very likely to die if treated with the older sera, whereas the other group was completely unselected and included all grades of severity; and (2) that much smaller doses were given to three-quarters of the patients given the new serum. All the patients receiving commercial antitoxin were given 120,000 units, whereas 12 of the 16 patients given the new serum received from an eighth to a third of this amount in antitoxic units. The organism was recovered from all of the 16 patients and was of the gravis type in 15; in the remaining case it was not typed.

CASE-RECORDS

The following is a sample of the case-notes of the patients receiving the avid serum.

CASE 1.—Male, aged 2¼ years. Grade 4. Fourth day of disease on admission. Bull neck. Membrane extensive, invading palate. Much faucial œdema. Nasal discharge profuse. Given 120,000 units avid serum, half intravenously. Membrane and nasal discharge clear in 4 days. Blood-pressure rose after administration of serum. Very faint trace of albumin in urine on 3rd, 4th and 19th day after admission; otherwise absent. No signs or symptoms of cardiovascular failure. No paralyses. Recovery uninterrupted. Discharged well.

CASE 2.—Female, aged 9¾ years. Grade 3. Late case, admitted 6th day of disease. Bull neck. Membrane very extensive, covering tonsils and palate and investing uvula. Urine loaded with albumin on admission. Given 104,000 units of avid serum. Throat clear and bull neck subsided in 4 days. Albumin in urine present in considerable amount on admission, gradually cleared and was absent 16 days after admission. Blood-pressure, after slight initial drop, rose about 10 days after admission and remained high thereafter. Multiple paralyses occurred, starting with palatal and ciliary paresis in 5th week, pharyngeal, diaphragmatic, neck and facial paralysis in 6th week and paralysis of extremities in 7th week. All these cleared up and no signs of cardiovascular failure supervened. Recovery was complete and patient was discharged well.

CASE 3.—Female, aged 9 years. Grade 4. Seen in consultation at 6 A.M. A little Jewess—a race peculiarly susceptible to diphtheria—and had been ill for 4 days. Very extensive membrane involving tonsils and soft palate, enormous faucial œdema and considerable subcutaneous bruisings. Enormous right-sided bull neck with the skin over it reddened, a very ominous sign in my experience. Profuse nasal discharge. Had been operated on the night before for a quinsy. Given 16,000 units of avid serum intravenously, repeated next day. Membrane cleared rather slowly, disappearing almost completely 6 days after admission and completely 2 days later. Nasal discharge dried up in 3 days. Bull neck took a week to subside. Albumin in urine for most of 6 weeks after admission. Blood-pressure fell slightly during first fortnight, but then rose to normal and remained so in spite of a palatal paresis which developed and cleared up in the 2nd week. Paralysis of the lower limbs and right side of the face developed in the 5th week but rapidly cleared up. No sign of cardiovascular failure. Recovery uninterrupted and patient discharged well.

CASE 4.—Male, aged 3 years. Grade 4. Fourth day of disease on admission. Extensive membrane covering tonsils and soft palate. Much faucial œdema. Huge bull neck. Hæmorrhage from throat and nose. Given 24,000 units avid serum, 8000 intramuscularly and 16,000 intravenously. Albumin in urine from 6th day, persisted. Throat very slow to clear. Hæmorrhages continued. Extremities cold. Pulse became irregular 4 days after admission and soon afterwards heart went into canter rhythm. Blood-pressure fell from 106 to 100, to 80 and to 72 during the 6 days in hospital. Albumin was present in the urine throughout. Child died on 6th day after admission. Did not live long enough to develop paralysis.

CASE 5.—Female, aged 7 years. Grade 4. Third day of disease on admission. Very extensive membrane covering tonsils, completely investing uvula and extending on to hard palate. Bull neck. Nasal discharge. Given 28,000 units avid serum, 8000 intramuscularly, 20,000 intravenously. Membrane cleared quickly; almost gone in 4 days and completely gone in 7 days. Nasal discharge clear in 4 days. Bull neck subsided in 6 days. No albumin in urine at any time. Blood-pressure fell very slightly in crucial period, but speedily returned to normal and remained so. No cardiovascular symptoms or signs and no paralysis. Recovery uninterrupted, and discharged well.

CASE 6.—Female, aged 1¾ years. Grade 3. Fourth day of disease on admission. Very extensive membrane covering both tonsils and soft palate and extending down posterior pharyngeal wall. Huge bull neck. Exceedingly toxic. Given 40,000 units avid serum, 8000 intramuscularly, 32,000 intravenously. Blood-pressure fell somewhat during first fortnight, but no cardiovascular symptoms or signs. Albumin in urine for few days and never in large amount. Apart from left internal squint which cleared up rapidly, no paralytic sequelæ, and convalescence rapid. Discharged well.

A FURTHER SERIES

When the supply of avid serum became exhausted we were able to conduct a further investigation. The Wellcome Physiological Research Laboratories sent us some more serum from the horse which had provided the avid serum, only this was taken at a much later stage of immunisation. The avidity of this serum was stated to be almost identical with that of commercial antitoxin. Up to date we have treated 20 unselected cases of hypertoxic diphtheria—9 of grade 3 and 11 of grade 4—with this non-avid serum, with 8 deaths, a case-fatality rate of 40%. All got maximal doses—that is, 120,000 units. These patients reacted in exactly the same way as those treated with commercial antitoxin. Membrane cleared slowly. Blood-pressure fell slightly after serum and steeply before cardiovascular failure set in. Cardiovascular sequelæ occurred with the usual frequency and were fatal in 6 of the cases in the first fortnight. The other 2 patients who died, after 35 and 49 days, had multiple paralyses, accompanied by late heart failure. Of the 6 patients who died of early heart failure 4 died with uncleared membrane on the throat. Albuminuria was common and tended to be persistent, bull necks subsided slowly. In short, this serum obtained from the same horse which had given the avid serum (i.e., the serum rich in Dr. O'Meara's anti-B factor) was ineffectual in treating hypertoxic diphtheria when it was known to be short of the anti-B factor.

COMMENTS

The single patient treated with avid serum who died (case 4) presented some interesting features. This was an undernourished child, but the main factor contributing to his death was hæmorrhages from the mucous membranes of the mouth and nose. The boy was given only 24,000 units of the new serum. Since then it has been suggested that hæmorrhage from the nose and throat and other mucous membranes seems to denote a greater degree of toxicity than subcutaneous hæmorrhage, and, looking back on the many hundreds of these cases that I have seen, I find that this is so. Whether this child would have recovered if given 60,000 or perhaps as much as 120,000 units of the avid serum, I do not know; I think it is doubtful.

Eight features in the clinical behaviour of the cases given the new serum are worthy of emphasis.

1. All—with one exception, the fatal case—failed to exhibit any symptoms of cardiovascular failure.

2. Clearing of the membrane from the throat and nose was very much accelerated.

3. Œdema of the throat disappeared much more rapidly than in patients treated with commercial antitoxin.
4. There was little or no albumin in the urine at any time.
5. In only a few patients were multiple paralytic sequelæ observed, and these recovered.
6. No late cardiovascular failure was seen even in the patients with multiple paralyses.
7. Bull neck disappeared often within 48 hours of administration of the new serum.
8. Blood-pressure, which usually falls fairly steeply during the first week after admission in cases treated with commercial antitoxin, did not fall to any extent in most of these cases, and in some actually rose after the administration of serum.

I have never before seen effects like these in hypertoxic diphtheria, and, since the only factor in treatment which was different in these 16 cases was the new serum, it is difficult to ascribe any other cause as responsible for the low mortality. The normal expectation of deaths in such a series was at least 6 and might have been 8.

SUMMARY

Cases of diphtheria at Cork Street Hospital are classified in 4 grades of severity. Grades 1 and 2 include faucial cases where the membrane is confined to the tonsils and its pillars, with or without laryngeal involvement, and pure laryngeal cases. Grades 3 and 4 are the "gravis" cases. In grade 3 the membrane extends on the palate, with faucial œdema and bull neck, and grade-4 cases show, in addition, hæmorrhages from mucous membranes and under the skin, with lesions in the nasopharynx.

The case-fatality rate in grades 1 and 2 is approximately 1%. In 259 successive cases of grades 3 and 4 treated with maximal doses of commercial antitoxin the case-fatality rate was 24·3% and in grade-4 cases alone was 46·5%.

A small quantity of antitoxin found to contain an abundance of O'Meara's "anti-B" factor was used to treat 16 hypertoxic cases of exceptional severity, 8 being of grade 3 and 8 of grade 4. The first 4 cases received maximal doses of 104,000–120,000 units, but in the remainder the dosage was reduced to 16,000–40,000 units. Only 1 of these 16 patients died. Except in the fatal case, there was no sign of cardiovascular failure and little fall in blood-pressure; membrane œdema and bull neck cleared rapidly.

A further group of 20 unselected and consecutive cases of hypertoxic diphtheria were given maximal doses of a serum, taken from the same horse which some months before had yielded the serum rich in anti-B factor. This control serum was known before use to contain very little anti-B factor and was described as "very little if at all different from ordinary commercial antitoxin." Among the cases receiving maximal doses of this non-avid serum there were 8 deaths, a fatality-rate of 40%.

It is concluded that an essential part of the treatment of hypertoxic diphtheria is the use of an avid serum rich in anti-B factor. The failure of commercial diphtheria antitoxin in the treatment of hypertoxic diphtheria hitherto is attributed to its poverty in anti-B factor.

As yet avid serum rich in anti-B factor cannot be produced at will.

I should like to acknowledge the great assistance of Dr. W. J. Roche, my senior assistant, in this work; also the help of Dr. J. A. Tynan, Dr. C. L. Joyce and Dr. M. I. O'Sullivan, my other assistants, and the staff of the Wellcome Physiological Research Laboratories. I am asked by Dr. J. W. Trevan of those laboratories to say that it is not possible at present to supply avid serum on demand.

The Edinburgh Medical Missionary Society has entered on its hundredth year and the occasion is to be commemorated by a service in St. Giles's Cathedral in May. At the annual meeting Mr. W. J. Stuart, F.R.C.S.E., who presided, said the war had affected the society's work at home and overseas. The ordinary income had fallen far short of expenditure, and a large deficit had only been averted by the use of legacies, which had been four times as great as usual. There were now 28 students on the society's roll, but there were no women students in the list. Mr. Stuart hoped that in subsequent years many women students would join the society as he was sure that there was work to be done in the Cowgate which could only be done by women.

FLUORINE IN THE ÆTIOLOGY OF ENDEMIC GOITRE

By Dagmar Curjel Wilson, M.D. Glasg., M.R.C.P., F.R.C.O.G., D.P.H.

WOMEN'S MEDICAL SERVICE, INDIA (RETD.)

Many different factors leading to relative or absolute deficiency of iodine may cause changes in the thyroid gland. May (1935) found that the administration of fluorine to rats produced hypoplasia of the thyroid epithelium with altered staining reaction of the colloid. Having experimented with over 800 patients, he advocated internal fluorine therapy in the treatment of toxic goitre. The evidence of alteration in thyroid structure in the experimental production of chronic fluorosis in animals is conflicting (Rohom 1937).

OBSERVATIONS IN INDIA AND ENGLAND

In making a clinical investigation of the occurrence of human dental fluorosis (Wilson 1939) I obtained a history of the existence of endemic goitre associated with cretinism in many areas where the presence of fluorine was recognised geologically. In North India a focus of endemic goitre has long been known in the Punjab plains (McCarrison 1913). The report of the Punjab government hospitals and dispensaries (1939) showed how numerous were the cases of goitre seeking treatment from this area. Macnamara (1880) studied the distribution of goitre in the Punjab plains before the introduction of the present extensive system of canal irrigation, at a time when the majority of the townspeople were dependent on local wells. In certain towns he found nearly all the inhabitants with goitre, and saw numerous cretins and dwarfs. Dogs and goats also had goitre. He observed that poverty and bad food led to increase in the size of the goitre, but noted that a colony of river fishermen did not show any thyroid enlargement. In this goitrous area of the Pubjab I observed a high degree of human dental fluorosis, as evidenced by mottled enamel among villagers still using well-water in the neighbourhood of Hundewali, where Heron (1913) found that the older Aravalli rocks emerge through the alluvium. Samples of these rocks were found to have a wide range of values for fluorine content, varying from 30 to 3200 parts per million. Geodetic investigations suggest that these older rocks extend between the Chenab and Ravi rivers, in an area coinciding with the downward extension of goitre in the Punjab plains.

In England the decrease of endemic goitre in recent times has been attributed to the improvement of village water-supplies and the closing of wells (Ash 1926). Cretinism was formerly associated with areas where the incidence of goitre was high (Norris 1848), but Joll, in 1932, found no focus of endemic cretinism remaining. Stocks (1928), reviewing the results of the Board of Education survey of goitre amongst English school-children, concluded that there was a belt where goitre was comparatively prevalent, extending, chiefly in rural areas, from Cornwall north-eastwards through Somerset, into Oxfordshire between the Cotswold and Chiltern hills, on into Northamptonshire, thence northwards to Derbyshire and up the Pennine chain. Orr (1931) named places in Cornwall, Somerset, Gloucester, Buckingham, Cumberland and Durham which were conspicuous in this respect.

MOTTLED ENAMEL

The geological outcrop of rocks containing fluorine has been described in England in Cornwall, Derbyshire, Cumberland and Durham (Carruthers and Pocock 1922), Somerset (Kingsbury 1939) and Buckingham (Bromehead 1940). The known distribution of fluorine in the soil of England, therefore, corresponds closely with the present or former distribution of endemic goitre, and I was interested to know whether the distribution in England of mottled enamel, as further evidence of the local occurrence of fluorine in the water, had any association with the distribution of endemic goitre. Inquiries were therefore made, and cases of dental fluorosis detected

among rural school-children using well-water in the neighbourhood of all known fluorine deposits. Mottled teeth were also found in villagers using well-water associated with the Oxford clay and to a less extent with the lias clay in Northampton, Oxford and Gloucester. In all those areas where dental fluorosis was present it was ascertained from the inhabitants that goitre still occurs.

I made a more detailed investigation of the state of the teeth of Somerset village children in a part of the rural district of Langport, in the neighbourhood of the villages of Charlton Mandeville and Long Sutton, two of the areas of high goitre incidence described by Stocks and by Young (1936), where the water-supply has remained unchanged from the time of their observations. In this area all the 378 children attending the seven local schools were examined. An adjoining area, the village of Somerton, not included by Stocks or Young in the area of endemic goitre, was selected as control, and all the 103 children in the two schools examined. The degree of dental fluorosis as manifested by mottling and staining of the enamel was recorded and graded according to the scale of Dean (1939).

In the control area the breadth of the thyroid gland of the school-children was measured as suggested by Stocks (1928), but in the goitrous areas treatment with iodides had been given, so that measurements of the thyroid were worthless as evidence. The breadth of the gland in the control area never exceeded 42 mm.; the normal breadth of the gland for children of comparable age always lies below this measurement. Thus there were no signs of endemic goitre among the control children.

Of the 378 children examined in the area previously mapped as goitrous, 55 showed some degree of dental fluorosis, while of the 103 children examined in the control area, none was affected (see table). Taking the

INCIDENCE OF DENTAL FLUOROSIS IN TWO GROUPS OF RURAL SCHOOL-CHILDREN, AGED 5–14 YEARS, IN A GOITROUS AND NON-GOITROUS AREA OF RURAL SOMERSET

Goitrous area						Control area. No thyroid enlargement	
Children examined	Number showing dental fluorosis					Children examined	Showing dental fluorosis
	F2	F3	F4	F5	Total		
378	25	21	7	2	55	103	0

Fluorosis is graded according to Dean (1938). F1 = normal; F2 = doubtful; F3 = very light; F4 = light; F5 = moderate (mottled); F6 = moderate (stained brown); F7 = somewhat serious; F8 = serious.

occurrence of dental fluorosis among the children as evidence, it can be concluded that fluorine is present in the drinking-water in two of the places in Somerset found by Stocks and by Young to be areas of high goitre incidence. The evidence identifying the presence of fluorine in drinking-water as one factor in the causation of endemic goitre is thus strengthened. I do not suggest, naturally, that this is the only factor, and fully realise that the intervention of other factors operating against the production of goitre may completely overcome the action of fluorine in promoting it. For instance, Young and others (1936) noticed that a weekly call by a fishmonger's van at an isolated village might completely counteract the effects of a local deficiency of iodine—an observation of interest in connexion with the low incidence of goitre found in the coastal areas of Essex where a high degree of human dental fluorosis has been described (Ainsworth 1933, Donaldson 1936).

SUMMARY

The distribution of endemic goitre in the Punjab and in England is related to the geological distribution of fluorine and to the distribution of human dental fluorosis (mottled enamel).

Inquiry showed the presence of dental fluorosis among school-children in two areas of Somerset where two previous observers had recorded a high incidence of goitre, and the absence of dental fluorosis in an adjoining area selected as control where endemic goitre was absent.

Observations in India were made during the course of nutritional investigations towards which financial assistance was received from the Royal Society. I am indebted to Mr. C. E. N. Bromehead, of the geological survey, and to Mr. P. Evans, geological department, Burmah Oil Co., for assistance on questions of geology; Dr. H. H. Green kindly analysed Kirana rock samples for fluorine; and Sir William Savage provided information about Somerset water-supplies.

This is the first of a series of studies of fluorosis.

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BRONCHITIS AND THE BRONCHIAL TREE

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CATARRH and inflammation of the respiratory passages must be considered in relation to the anatomical structure of the bronchial tree, the distinction between bronchi and bronchioles, and the peculiarities of the mucous membrane and its glands. In the study described here we used sections through the whole lung of infants and young children, and thus obtained a general picture of the distribution of the glands in relation to the bronchial tree. The lungs were fixed by the intravenous injection of formalin saline.

BRONCHI AND BRONCHIOLES

The term "bronchiole" is customarily reserved for tubes with a diameter of less than 1 mm., but the structure of the wall and the relationship to neighbouring lung tissue are more characteristic than mere size. Bronchi have thick fibrous walls permeated by elastic fibres and reinforced by cartilage; the epithelium of the mucous membrane is arranged in basal, intermediate and columnar layers, and goblet cells are numerous; glands are embedded in the deeper layers of the mucous membrane. The bronchi run in the interstitial connective tissue of the lung which separates them from the lung itself, they are, so to speak, extrapulmonary. Bronchioles, on the other hand, have thin walls devoid of glands, and are embedded directly in the lung tissue of which they are a part. The larger bronchioles have minute cartilages supporting their angles of division, but otherwise the walls contain no cartilage. They are lined with basal and columnar epithelium only; goblet cells are few in all bronchioles and absent in the smallest. The bronchi are kept patent by their strong cartilaginous wall, the bronchioles partly by the tone of the muscle in their walls, but chiefly by the respiratory movements which distend them as well as the air-spaces. The general arrangement of the bronchial tree is shown in fig. 1.

THE GLANDS

Textbooks and even recent monographs (e.g. Miller and Policard[1]) make scanty reference to the histology

1. Miller, W. S. The Lung, London, 1937. Policard, A. Le Poumon, Paris, 1938.

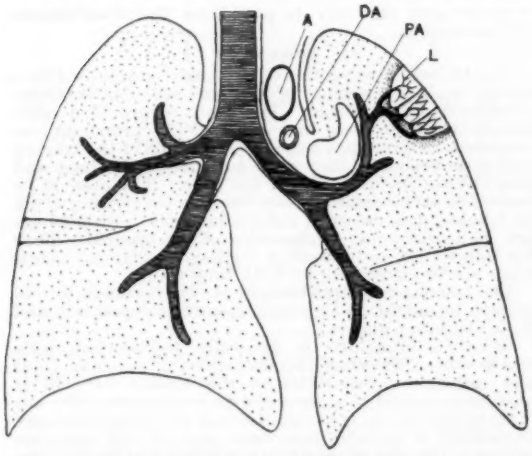

FIG. 1—Coronal section through both lungs of an infant aged 8 months. The lobules marked in the left upper lobe are correct in size and situation, and are chosen as a simple example of individual lobules in the periphery. The bronchi are marked by double or heavy outlines and by shading, the bronchioli by simple lines. Semidiagrammatic (life size). A, aorta; DA, ductus arteriosus; PA, pulmonary artery; L, lobule.

of the glands. We propose to describe their arrangement in four regions: the trachea and main bronchi; the large bronchi; the medium and small bronchi; and the bronchioles. In the trachea and main bronchi glands are abundant. The individual gland complexes are so large and so close together that they form a continuous coat between the lamina propria and the cartilage, and even invade the spaces between the cartilaginous rings, spreading out beyond them like a mushroom. The large bronchi—that is, the first few subdivisions of the main bronchi—though less rich in glands are well supplied. The glands no longer form a continuous layer, but are aggregated into separate masses, the shape and size of which vary with the space available (fig. 2). They are sometimes internal, sometimes external, to the cartilages and sometimes lie between them. The glands decrease considerably in number and size in the medium and small bronchi. The reduction runs parallel with the reduction in calibre of the bronchi and the diminution of cartilage content. Bronchioles have neither cartilage nor glands in their wall. Goblet cells in normal bronchial epithelium are not very numerous; when the epithelium is irritated, however, they may increase rapidly in number and sometimes almost every columnar cell may be replaced by a goblet cell. The abundance of goblet cells in pathological cases shows that every columnar cell in the bronchial tubes is capable of being converted into a goblet cell.

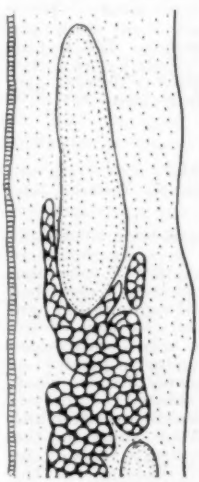

FIG. 2—Camera lucida tracing showing the glands in a bronchus 3 mm. in diameter of a child aged 4 years. Longitudinal section (× 15).

In the newborn infant the glandular apparatus is underdeveloped throughout the bronchial tree. It takes some months for the glands to reach maturity and full size. The first buds from the lining epithelium appear towards the end of the fourth fœtal month, and by birth some gland tissue is present. Growth continues during the first few months of life and at 5–6 months the gland tissue appears to be adequate. The illustration (fig. 3, a, b, c) was taken from the trachea because glands are most abundant there.

SECRETION

In considering the *function* of the mucous membrane and the glands, it must be remembered that the secreting surface of the abundant glandular tissue in the trachea and large bronchi is much greater than that of the mucous membrane itself. The glands secrete fluid which has a function similar to that of the lacrimal glands; it serves to moisten the enormous inner surface of the lung and its bronchi and bronchioles. In view of the continuous rhythmical flow of air the amount of fluid required is considerable. The combined activity of the goblet cells and the glands keeps the mucous membrane covered with a moist, slightly viscous coating. A secondary and vitally important function of the secretion is to cleanse the inhaled air. The air is cleansed of dust and organisms by the respiratory passages themselves; otherwise, the lung being a cul-de-sac, the respiratory tissue would be damaged or continually exposed to infection. The harmful effects of excessive influx of dust are demonstrated in pneumoconiosis. The viscous lining of the air passages traps particles and they are eliminated with the mucus; this occurs chiefly in the trachea and large bronchi. Particles which evade them may well be caught in the smaller bronchi which are also provided with glands. Only a small proportion of the particles entering

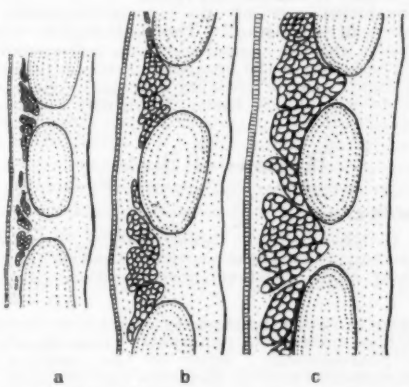

FIG. 3—Camera lucida tracings of the trachea of infants of 3 weeks, 3 and 8 months. The drawings show the increasing amount of gland-tissue, both absolutely and also relatively to the thickness of the wall. Longitudinal sections (× 15).

the trachea reach the respiratory tissue and are dealt with there. In pathological irritation of the respiratory passages not only are the goblet cells increased in number, but the glands become mucus-secreting in type and the quantity of mucus produced rises appreciably, especially in the trachea and large bronchi where most of the glands are congregated.

TRACHEO-BRONCHITIS, BRONCHITIS AND BRONCHIOLITIS

The structural differences between bronchi and bronchioles and their different relationship to the lung tissue make it inevitable that there must be a fundamental difference between tracheitis and bronchitis on the one hand, and bronchiolitis on the other. The two former are extrapulmonary but bronchiolitis is an intrapulmonary condition. Tracheitis and bronchitis affect thick-walled tubes, bronchiolitis tubes with delicate walls in direct contact with lung tissue. Bronchiolitis is therefore more serious than the other two conditions and the prognosis is always uncertain. The first impact of infection naturally falls on the upper part of the bronchial tree, which, in virtue of its abundant glands, is most capable of reacting effectively. Over-secretion produces the clinical signs of catarrh or tracheo-bronchitis. The infecting agent is arrested before it reaches deeper and more vulnerable regions. Ordinary slight infections—mild influenza and the common cold—are dealt with in this way. The pathology of tracheo-bronchitis is thus rarely seen, but we were able to study it in 2 children who had died of non-respiratory diseases.

The trachea and large bronchi were thickly covered with yellow mucus which stopped abruptly at the hilar region. The distribution of the glands and the fact that catarrh is often localised to the trachea and large bronchi suggests that the massed glands form a barrier against lung infection. There is a widespread tendency to consider that the smaller bronchi are the site of infection in ordinary coughs, hence the diagnosis of bronchitis. This misconception may lead to the wrong prognosis and treatment.

Bronchitis affecting the smaller bronchial tubes, either restricted to one area or generalised throughout the lung, is much rarer than tracheo-bronchitis. It may arise as a separate entity, or in the course of a general infection such as measles, and prognosis and treatment are different from those of tracheo-bronchitis. Secretion in the trachea and large bronchi does not seriously hinder respiration; the mucus is easily expectorated and has only a short distance to travel. Mucus in the smaller bronchi is far more likely to cause obstruction and expectoration becomes more difficult as the diameter of the tubes decreases; and the younger the child the smaller the average lumen of the tubes. Bronchiolitis differs completely from both tracheo-bronchitis and bronchitis, in which even in serious cases only the mucous membrane is affected; lesions of the deeper layers of the wall occur only in exceptional cases.

In bronchiolitis not only the mucous membrane but the whole wall is inflamed. The pathological changes are extensive and the clinical condition correspondingly grave. The lumen of the bronchiole becomes narrowed, its wall rigid and its mobility impaired. Secondary collapse of the lung tissue frequently occurs as a result and the way is paved for the development of pneumonia.

SUMMARY

The bronchi, irrespective of size, are characterised by a strong wall, consisting of fibrous and elastic tissue reinforced by cartilage. The wall is provided with glands which decrease in number as the bronchial tree branches. Glands are specially abundant in the trachea and main bronchi; they serve to moisten the lung and also cleanse the air entering the lung. The bronchi lie in the fibrous interstitial tissue between the lung segments or lobules, and are thus extrapulmonary. Bronchioles are the intralobular continuation of the bronchi. They are thin-walled and devoid of cartilage or glands. Their walls are in direct contact with lung tissue.

The trachea and large bronchi are the favourite site of catarrh as might be expected from their position and their abundant glands.

So-called bronchitis is generally tracheo-bronchitis and is one of the chief manifestations of common colds and influenza. Bronchitis of the smaller bronchi is uncommoner and prognosis and treatment are different.

Bronchiolitis, in contradistinction to extrapulmonary bronchitis, is an intrapulmonary process and therefore serious. Its chief characteristic is inflammatory involvement of the whole wall of the bronchiole.

These investigations were begun many years ago by one of us (S. E.) and have been completed at the Hospital for Sick Children, Great Ormond Street. We are indebted to the medical committee who afforded us the opportunity to carry them out, and to Dr. D. Nabarro, late director of the pathological department, for his help.

Reviews of Books

Pharmacology

By J. H. GADDUM, Sc.D. Camb., M.R.C.S., professor of pharmacology in the University of London. London: Humphrey Milford, Oxford University Press. Pp. 407. 17*s.* 6*d.*

NOTWITHSTANDING the modesty of the title Professor Gaddum here embraces a remarkable range of subjects akin to pharmacology. Many of the chapters are excellent, notably those on hormones and vitamins, and there is a valuable discussion of diet, salts and fats. Dr. Gaddum writes on these topics as one with authority. These are the advances which in the past few decades have crystallised out of the mother liquor of experimental physiology. They have a sharpness of outline which stands out in striking contrast against a background of lustreless empiricism. Professor Gaddum handles his material with a lightness of touch which is as welcome as it is unusual in textbooks on this subject. But what we gain on the pharmacological roundabouts we lose on the therapeutic swings. Indeed, when he discusses clinical aspects the author betrays some uneasiness. In the section on digitalis, for example, he says that in auricular fibrillation the auricle is *beating* very rapidly. The brief account of the response of the patient with auricular fibrillation to digitalisation is inadequate, and no mention is made of the value of digitalis in cases of cardiac insufficiency associated with normal rhythm, nor of its use in aortic regurgitation with cardiac failure. More than two pages are given to the toxicology of lead, but no reference is made to the therapeutic value of the official preparations of lead acetate. Professor Gaddum has been no more successful than his predecessors in his attempt to improve on the old-fashioned arrangement of the materia medica founded on Schmiedeberg's classification. The "systems"—nervous, alimentary, circulatory—have been used, but the method is abandoned in order to introduce chapters on such important subjects as the heavy metals, disinfectants and proteins. This would be of little moment if it did not involve the use of a vast amount of cross reference which becomes tedious for the reader. All in all the book contains a great deal of information not readily available elsewhere. The final chapter, with its sections on the combined effects of two drugs, biological assay, and therapeutic trials in man, deserves high praise.

Heart Failure

(2nd ed.) By ARTHUR M. FISHBERG, M.D., associate in medicine, Mount Sinai Hospital, New York City. London: Henry Kimpton. Pp. 829. 40*s.*

INTERPRETING "heart failure" in a very liberal manner, Dr. Fishberg has brought together a remarkably complete and balanced collection of facts. It is no mere list, but a reasoned exposition of the subject by one who has wide clinical experience and who has played a notable part in recent laboratory investigations. He presents even the most difficult aspects of his subject in a form which makes them clear to the clinician lacking experience of research technique. Essentially clinical in its outlook, the book ably correlates experimental and clinical findings, and the author seldom attempts to carry this process further than the facts justify. When correlation is impossible he admits it at once and theorising is never carried to extremes. The instant success of this work was not only a tribute to the author but also a demonstration that it filled a definite gap. The new edition has been thoroughly revised.

X Rays

Their Origin, Dosage, and Practical Application. (5th ed.) By W. E. SCHALL, B.Sc. Lond., F.Inst.P. Bristol: John Wright and Son. Pp. 252. 15*s.*

Mr. Schall has enlarged his practical book with some of the more recent developments in construction of tubes and measurements of the quantity of radiation. There is a useful section in which apparatus is described from the point of view of the electrical engineer and here there are valuable descriptions of the new type of hot cathode and rotating anode X-ray tubes, with some helpful rating curves. The elementary physics of radiation are discussed and the explanations are clear, although it is really impossible to condense the analysis of such complex processes as characteristic radiation and absorption without omitting essential steps in the reasoning. The book contains references to most of the subjects required by radiographers studying for the M.S.R., and is readable; the inclusion of a number of tables both of physical constants and of X-ray exposures and depth doses make it a useful book of reference. It is profusely illustrated with diagrams and photographs of instruments and apparatus made by Schall and Sons Ltd.

THE LANCET

LONDON: SATURDAY, FEBRUARY 15, 1941

DIPHTHERIA ANTITOXIN

THE discovery of diphtheria antitoxin marked a peak in the story of therapeutics, and its usefulness is universally accepted, but recent happenings are raising doubts whether present supplies are as effective as our knowledge can make them. The serum producer has been impelled to make ever more attractive antitoxin, and the measure of its attractiveness has been the smallness of the volume containing the required number of Ehrlich "units," which are based on the amount of antitoxin required to save the life of a guineapig imperilled by a fatal dose of toxin. Parallel with this effort has marched an attempt to remove the tendency of injected serum to cause the familiar reaction, with its urticaria, joint-pains and fever. There have been three stages in the development of modern antitoxin. In the first, the unaltered serum of the immunised horse was used, which produced reactions in perhaps 40% of patients; in the second, much useless material containing little or none of the Ehrlich antitoxin was removed by precipitation with ammonium sulphate, and reactions now occurred in about 20%; in the third and present stage, the work of PARFENTJEF and POPE has provided partially digested varieties of antitoxin with increased unitage and scarcely any tendency to cause reactions. Have these achievements yielded therapeutically better serum? Certain immunological rebels have at times attacked the accepted beliefs and complained that all these manipulations have given us a sophisticated product not so helpful to the patient as the old.

One of the mysterious properties of antitoxin is that called "avidity." The nature of the union of antitoxin and toxin has not yet been explained to the satisfaction of the physical and molecular chemists, but certain crude facts are known. MADSEN stressed the time factor, and his "highly avid" serum seized the available toxin with great speed; GLENNY emphasised the firmness of the bond. It is possible for the serologist to choose a row of diphtheria antitoxins produced in the same establishment by the same methods, and identical in value by the Ehrlich test, but divisible into MADSEN'S fast-combining and slow-combining groups, and these groups can again be divided into GLENNY'S firmly combined and loosely combined groups. The complexities facing the inquirer on this subject may be judged from one experiment. A rabbit may be given intravenously a certain mixture of diphtheria toxin and non-acid antitoxin and lives on undisturbed. A similar rabbit injected intravenously with but a tenth of the same mixture dies of diphtheria toxæmia in a few days. A third rabbit injected with a few c.cm. of the blood of the first unharmed rabbit also dies typically in a few days. The explanation of this seeming paradox is that the combination between toxin and non-avid antitoxin is not a firm one, so that when the neutral mixture is sufficiently diluted with the rabbit's blood the toxin is set free. Do avid sera possess some peculiar therapeutic virtue? Dr. O'MEARA and Dr. MCSWEENEY, whose papers appear in this issue, believe that they do. The latter tells of one death among sixteen cases of diphtheria in the severe grades 3 and 4 when treated with a highly avid serum, while the expected fatality would have been four cases. The statistician may see nothing remarkable in a run of sixteen cases without a death, but Dr. MCSWEENEY points out the other striking features of this series—the rarity of fall in blood-pressure or cardiovascular failure, the absence of albuminuria or residual paralyses, and the rapid disappearance of membrane and bull-neck. He says that never before—and he has had great experience—has he seen effects like these in hypertoxic cases, and that it is difficult to avoid crediting the avid serum with them. Dr. O'MEARA advances an attractive elucidation of these clinical results. On his hypothesis the diphtheria bacillus in the body produces two factors—substance A, highly toxic to guineapigs and toxic to patients; and substance B, a second antigen which may itself be toxic to children and may also allow substance A to penetrate deeply and damaged tissue. Whether substance B is identical with MCLEAN'S preparation of Duran-Reynals diffusion factor from the diphtheria bacillus is a question yet to be answered. The second claim in the hypothesis is that avid antitoxin contains, as well as anti-A, a substantial amount of anti-B antibody, and hence its therapeutic efficiency in hypertoxic cases where both A and B are at work. On the other hand, ordinary commercial antitoxin, which is prepared from horses injected with the toxin of Park-Williams No. 8 strain, a "mitis" strain poor in substance B, contains little or none of anti-B and is therefore ineffective against hypertoxic diphtheria.

The next step should be to test the avid serum on a large number of hypertoxic cases in Dublin and elsewhere, but no more of the serum is available, though an attempt is of course being made to prepare it. The serum used by Dr. MCSWEENEY was a freak; it was produced by the ordinary methods of immunisation and made its appearance in one horse by chance. We are entitled to ask the Dublin observers for experimental evidence that this freak serum did contain much antitoxin to pure B toxin, and that the later non-avid serum from the same horse contained little or none. At present it is not clear why the desired antitoxin has not been made by using pure B toxin, as MCLEAN produced antidiffusing sera with purified bacterial diffusing solutions. Meanwhile, whether or not Dr. O'MEARA'S hypothesis stands the test of time and further experimental examination, his work may stimulate clinicians to collaborate with serum producers.

ADSORBENTS

FAITH, we are assured on the highest authority, is the substance of things hoped for. In no branch of therapeutics is this better illustrated than in the clinical application of adsorbents. Although they must be numbered among our oldest drugs, their pharmacological actions in man remain obscure, and their continued use is based partly on empiricism and partly on highly spectacular experiments in vitro. The growing popularity of the adsorbents among the lay public is probably the outcome of the modern cult for "inner cleanliness," for we live in an age when every newspaper reader is haunted by the thought

that he is "a goodly apple rotten at the heart." The use of drugs which have a physical rather than a chemical action makes a strong appeal to most physicians susceptible to the golden rule that the doctor should do no harm. It would be foolish to exaggerate the dangers associated with the presence of adsorbents in the alimentary canal, but it is none the less true that these substances are not entirely innocuous. MUTCH[1] has shown that kaolins differ a good deal in quality and his microphotographs of the gritty particles obtained from kaolin, B.P. and from a purified proprietary kaolin immediately suggest the potential dangers of taking these preparations for long periods. We have previously referred[2] to EMERY'S[3] observations regarding the traumatic and mechanical sequelæ arising out of the use of adsorbents; and as we may yet have to cope with epidemics of dysentery it is worth while to recall that during the last war the Germans discarded the use of kaolin because of the development of fatal perforations.[4]

The therapeutic potency of adsorbents varies almost as widely as their purity. Quoting investigations by RAE and HELLMUT MÜLLER, MUTCH records that German kaolin would not remove more than 50% of mussel poison from an aqueous solution and that activated charcoal failed to remove any at all. On the other hand, the English variety of kaolin used in MUTCH'S experiments removed the toxic substances completely. This variability of efficiency is partly due to the operation of physical conditions, often overlooked, such as the tendency of some kaolins to coalesce by mutual flocculation because of the presence of uncompensated electrolytes. MUTCH has also shown that it is impossible to deduce the therapeutic potency of an adsorbent from its ability to adsorb dyes, and he stresses the importance of measuring the power of the adsorbents to fix material of clinical significance, such as known food poisons.

It has been known for a long time that the adsorbents rapidly remove alkaloidal salts from solutions; and when kaolin is administered with morphine preparations the alkaloid is largely adsorbed on to the inert material. This state lasts as long as the kaolin remains in the strongly acid medium of the stomach, but as the adsorbent travels through the intestine, where the pH rises, the alkaloid is gradually liberated and a sustained morphine effect is achieved. Thus in this form of therapy variation of the H-ion concentration exerts a desirable action whether it is intended or not. If the same thing happen when adsorbents are used to fix food poisons and bacteria, it follows that kaolin and similar substances should be employed merely as a preliminary to washing out the stomach or the administration of rapidly acting purgatives. Their use, in fact, corresponds fundamentally to the administration of tannic acid as an antidote in poisoning by salts of the heavy metals; the tannate must be removed lest it be "digested" and absorbed. This conception of the influence of adsorbents may be refuted by further research, which may show that fixation is practically permanent. If so, it must be borne in mind that the process of adsorption in the alimentary canal is indiscriminate; not only noxious agents but also physiological substances such as enzymes, vitamins and mucus are liable to be prevented from performing their proper functions. MESSERLI'S experimental work lends support to this possibility. He has shown[5] that rats and pigeons fed on a diet of decorticated rice developed an avitaminosis more rapidly and more severely if charcoal or kaolin was mixed in the diet. When adsorbents are taken by the human subject over a short period of a few days or weeks these effects are probably negligible, but in the case of patients with chronic alimentary diseases such as colitis and peptic ulcer, frequent and prolonged administration of adsorbents may produce symptoms of deficiency disease. There is a growing practice to substitute adsorbents, especially hydrated magnesium trisilicate, for chemical neutralisers of gastric acidity, because neutralisation is better than alkalinisation, and a more prolonged effect can be obtained. Undoubtedly a good case can be made out for this preference, but it would appear that insufficient attention has been paid to the possible harmful effects that adsorbents may have upon digestive and nutritive processes in the bowel. In this connexion, even liquid paraffin has been called in question,[6] and the paraffin addict who is on a borderline diet may be parting with a significant proportion of his fat-soluble vitamins every time he passes an oily motion. Anything which might interfere with the proper utilisation of the vitamin content of our present diet is a potential danger, and this aspect of adsorbent therapy would repay further study.

1. Mutch, N. *Brit. med. J.* 1937, **1**, 595.
2. *Lancet*, 1937, **1**, 452.
3. Emery, E. S. *J. Amer. med. Ass.* 1937, **108**, 202.
4. *Ibid*, 1930, **94**, 1406.

ENDEMIC FLUOROSIS

THE bones of marine mammals and their evolutionary ancestors are many times richer in the halogen fluorine than those of land mammals. In man it normally enters into cell metabolism to a small extent, but when taken in quantities which might be harmless to the whale and the porpoise may have pathological effects ranging from "mottled teeth" to calcification of tendons, ligaments and fasciæ, or to osteophytic formation which according to ROHOLM[7] may progress to synostosis of joints, especially those of the vertebral column. The first cases in Great Britain of industrial disease associated with fluorine were recorded in Sheffield last year by WILKIE.[8] Fluorosis of milder degree, leading to mottling of the teeth, is endemic in some parts of Great Britain and was first noted by AINSWORTH[9] at Maldon in Essex. The discoloration appears as opaque white or brownish patches on the enamel and is likely to occur in those who drink water containing more than 4·5 parts per million of fluorine. Evidence is accumulating to show that dietary deficiencies may aggravate the effects of fluorine,[10] and PIERCE[11] found that signs of fluorosis were enhanced in poorly nourished sheep. In South India, SHORTT and his colleagues[12] found mottled teeth and painful skeletal deformities among the rice-eating peasantry; their animals, taking rice straw as fodder, were also affected. In North India, where the people eat the more

5. Messerli, N. *Arch. int. Physiol.* 1922, **19**, 103.
6. See *Lancet*, 1940, **2**, 559.
7. Roholm, K. Fluorine Intoxication, London, 1937.
8. Wilkie, *J. Brit. J. Radiol.* 1940, **13**, 213.
9. Ainsworth, N. *J. Brit. dent. J.* 1933, **55**, 233.
10. Smith, M. E. Lantz, E. M. and Smith, H. V. *Univ. Arizona tech. Bull.* 1931, No. 32.
11. Pierce, A. W. *Nutr. Abstr. Rev.* 1939, **2**, 253.
12. Shortt, H. E., McRobert, G. R., Barnard, T. W. and Mayar, A. S. M. *Ind. J. med. Res.* 1937, **25**, 553.

nutritious wheat and use its straw as fodder, WILSON[13] found places where mottled teeth were common and severe, but where skeletal deformity only occurred among the poorest and worst-fed villagers, and was rare among the animals.

Evidence that drinking-water may be the source of the fluorine is fairly convincing. In the United States DEAN and his colleagues[14] have shown that if water devoid of fluorine is substituted in affected regions no further cases of fluorosis develop. They also noted, in comparing two groups of children, that a lower incidence of caries was associated with a higher fluorine content of the water. The problem of fluorosis is evidently entangled with several others; WILSON, whose paper appears on another page, has found, both in England and India, that in regions where the presence of fluorine has been demonstrated in the soil goitre and cretinism are—or have been—endemic; and has found in such regions a high degree of dental fluorosis among villagers using well-water. This raises some diverting speculation: fluorine may be capable, for example, of ousting its more lethargic cousin, iodine, from its essential place in thyroid metabolism. One aspect of the problem is clearly geological. The usual fluorine-bearing mineral is fluorspar or fluorite; as it is a highly insoluble fluoride of calcium there is no evidence to incriminate it as a cause of the condition. Fluorapatite, a calcium fluophosphate, is present in small quantities in many sedimentary rocks such as sands and sandstones, and might where exceptionally abundant affect drinking-water derived from these strata. But data for deciding this point are imperfect; among the vast numbers of analyses of drinking-water carried out in Great Britain attempts to estimate the fluorine content are uncommon. In Somerset fluorspar is very rare, and only occurs in small isolated patches in the Mendips; and there is no reason to suspect unusual concentrations of fluorapatite. Of 27 fluorosis localities detected by WILSON in Somerset, 20 are situated in the lias formation; and this distribution suggests that the lias or some formation closely beneath it is the geological source of the condition, at any rate in Somerset. Many of WILSON's patients had used water from wells dug in the lower lias clays. The fluorine may be present in these clays or may be concentrated just below in a thin bed full of the fossil remains of marine vertebrate animals—the rhætic bone bed. There is evidence from other localities for thinking that the fluorine causing fluorosis is present in clays, especially those containing marine vertebrate remains; and it may find its way into the human subject either from drinking-water obtained from wells in these clays or possibly from the fumes from kilns in which the clays are baked into bricks.

These suggested origins of the condition in teeth and bones, however, are no more than a plausible guess at present. VAN DER MERWE[15] has described means for measuring traces of fluorine in natural waters and he and NICHOLS[16] have discussed methods for treating domestic water-supplies containing excess of fluorine. Dentists and doctors who encounter cases of fluorosis can help to settle the origin of the fluorine by finding out when the condition arose and what water the patient was drinking at the time. If they will then have the fluorine content of the water estimated by an analyst and send the results to the Director of the Geological Survey* it will be possible to say more certainly which geological horizons are dangerous and how the condition may be eradicated.

13. Wilson, D. C. *Nature, Lond.* 1939, **144**, 155.
14. Dean, H. T., Jay, P., Arnold, F. A. McClure, F. J. and Elvove, E. *Publ. Hlth Rep., Wash.* 1939, **54**, 862.
15. Van der Merwe, P. K. *Anderstepoort J.* 1940, **14**, 335.
16. Nichols, M. S. *Amer. J. publ. Hlth*, 1939, **29**, 991.

Annotations

A PROMISING NEW SULPHONAMIDE

THE effects on laboratory animals of sulphadiazine (2 sulphanilamidopyrimidine), one of the latest additions to the sulphonamide family, have been studied by Feinstone and his colleagues[1] at Johns Hopkins. The new compound results from the replacement of one hydrogen atom in the sulphonamide group of sulphanilamide by a pyrimidine ring. As in sulphapyridine and sulphathiazole it is a heterocyclic ring which is introduced into the molecule. The most striking feature of this compound is the high concentration in the blood which is obtained even after a single dose by mouth—higher than is obtained after sulphapyridine. Thus in the rabbit, after a single dose of 0·25 g. per kg. body-weight, the total concentration of free and combined sulphadiazine in the blood rose to 21 mg. per 100 c.cm.; sulphapyridine gave 13 mg. per 100 c.cm. Other animals gave comparable results. The speed of absorption appears to vary with the species of animal used, but in most cases the concentration in the blood was nearly maximum in an hour. There are two ways in which the effects (toxic or therapeutic) of members of the sulphonamide family may be compared. Either the animals may be given the same dosage of the different drugs or the dosages may be varied so that the blood concentrations of the different drugs remain equal. Using equal dosages Feinstone and his fellow workers found sulphadiazine to be more toxic to mice than sulphathiazole, which in turn was more toxic than sulphapyridine or sulphanilamide. Towards monkeys either with equal dosage or with equal concentrations in the blood, sulphadiazine seemed to be less toxic than sulphapyridine. They found that in the monkey the proportion of the drug present in the bloodstream as the acetyl derivative was much greater in the case of sulphapyridine than in the case of sulphadiazine; it is known that the acetyl derivative of sulphapyridine is more toxic than the drug itself and the apparent greater toxicity of sulphapyridine might perhaps be due to the greater amount of acetyl derivative. They found, too, that deposits of crystals of the acetyl derivative commonly appeared in the urinary tract after high-blood concentrations of sulphapyridine and less frequently with sulphadiazine. With increasing recognition of the need for adequate dosage of sulphapyridine the danger of the formation of such deposits is increased.

The observations on the therapeutic value of the new compound are not conclusive because only the results of equal dosages of the different drugs were compared, and with equal dosages sulphadiazine gives higher concentrations in the blood. However, if the human body can tolerate higher blood concentrations of sulphadiazine than of other members of the series the results are still of value. Only mice were used in these experiments. In the treatment of streptococcal and pneumococcal infections sulphadiazine gave results comparable to those given by sulphanilamide and sulphapyridine; the results in staphylococcal infection were similar to those of sulphathiazole. Against infection of the mice with Friedländer's bacillus strain B, sulphadiazine was much more effective than either sulphanilamide, sulphapyri-

* Exhibition Road, London, S.W.7.

1. Feinstone, W. H., Williams, R. D., Wolff, R. T., Huntington, E. and Crossley, M. L. *Bull. Johns Hopk. Hosp.* 1940, **67**, 427.

dine or sulphathiazole. If this proves to be the case for all strains of Friedländer's bacillus in human infections, then sulphadiazine has at once a place in therapeutics; opinions differ on the value of the chemotherapeutic agents used hitherto in this infection but agree that there is room for improvement.

THE PELVIC JOINTS IN PREGNANCY

As long ago as the time of Hippocrates it was taught that the pelvic joints underwent relaxation, the resultant enlargement of the pelvic capacity facilitating delivery. Ambroise Paré subscribed to this theory of disjunctio pelvica, though Vesalius protested against the view. A considerable bibliography has accumulated on this subject, and recently Prof. James Young[1] has reinvestigated it. Using a technique of radiological mensuration he has established that the pubic and sacro-iliac joints of pregnant women, when compared with non-pregnant controls, undergo a significant expansion. In the case of the sacro-iliac joints the figure for joint space is 4·5 mm. compared with a normal reading of 3·6–3·9 mm., and in the case of the pubic symphysis 4·2–5 mm. compared with 2·6 mm. From his studies he has reached several important conclusions: that pregnancy leads to a relaxation of the pubic joints; that this disjunction may assume pathological extent and lead to a subluxation; that labour is not the cause, since the increase in joint space is apparent in the first half of pregnancy; that the joint involutes to the pre-pregnant state by the end of the 3rd to 6th month after delivery; and that parity has no significant effect on the changes, primiparæ and multiparæ being affected to an equal degree. The changes are more easily demonstrable in the symphysis than in the sacro-iliac joints, though both are similarly affected. The ætiology of this joint relaxation has been carefully studied by Hisaw[2] in rabbits; he concluded that a hormone, relaxin, was responsible, and he was able to produce this joint change by injection of relaxin into virgin rabbits in œstrus. The physiological significance of this work as far as pregnant women is concerned, though small, is a two-fold one. The relaxation of the pelvic joints very slightly increases pelvic capacity, and the forward rotation of the pelvis on the sacrum increases the anteroposterior diameter of the inlet, a fact that led to the adoption of Walcher's position for short periods to encourage a refractory fœtal head to engage in the pelvis in the first stage of labour. By the same token the squatting position operating in the reverse way should facilitate the passage of the head through the outlet at the end of the second stage, a fact well known among primitive races, whose womenfolk favour this position for delivery. Professor Young is chiefly interested in two aspects of this work. First, that in a small proportion of women—0·75% or 34 out of 4512 deliveries—the relaxation has progressed to a pathological subluxation of the symphysis, in which the two halves of the pelvis were freely movable, resulting in a painful waddling gait or complete disability requiring treatment in bed. Such a condition is predisposed to by some intercurrent disease (in Professor Young's series this was seen in 38·2%) and by the postural strain induced by an alteration in the normal spinal curves due to the lordosis induced by the weight of the gravid uterus. His second interest is the persistence of backache in the delivered woman and the significance of this arthropathy of pregnancy in its ætiology. He found backache to be present in 46·6% of cases suffering from the combined pubic and sacro-iliac lesion in a careful follow-up investigation. Regarding treatment he found that forcible manipulation gave excellent results in two-thirds of these cases.

The lesson to be learned from Professor Young's paper is that the pregnant woman who complains of backache or pain over the symphysis should be carefully investigated by radiology and shielded from unnecessary trauma to the affected joints, so that she may be insured against that unpleasant legacy of a confinement, persistent low backache, from sacro-iliac strain, a disability that causes much economic and psychological damage among the child-bearing population. Rest, physiotherapy and a properly fitting corset will do much to alleviate the strain on the relaxed joints in the puerperium until such time as nature has completed their proper involution.

1. *J. Obstet. Gynæc.* 1940, **47**, 493.
2. Hisaw, F. L. *Proc. Soc. exp. Biol., N.Y.* 1926, **23**, 661.

HYPOGLYCÆMIA

HYPOGLYCÆMIA as a rule arises from hyperinsulinism whether endogenous (from overaction of the pancreatic islet cells usually associated with an adenoma) or exogenous (from an overdose of insulin), but it is not always realised that the symptoms of hypoglycæmia may occur without hyperinsulinism, and they may then be attributed to epilepsy, narcolepsy, intracranial tumour, psychosis, psychoneurosis, neurasthenia and gastro-intestinal disturbances, particularly peptic ulcer. The finding of a low blood-sugar value, however, does not necessarily mean that this is the explanation of the symptoms, for low fasting values are obtained in normal people on a low carbohydrate diet as well as in anorexia nervosa, Simmonds's disease and idiopathic steatorrhœa, without the symptoms of hypoglycæmia. For the diagnosis of hypoglycæmia it is essential that in addition to the low blood-sugar value the symptoms shall be relieved by the administration of dextrose. Conn[1] has classified the ætiological factors of spontaneous hypoglycæmia into two main groups. The organic group, with a recognisable anatomical lesion, includes hyperinsulinism arising from the pancreas, hepatic disease, pituitary and adrenal hypofunction, and lesions of the central nervous system. The functional group, with no recognisable anatomical lesion, includes certain cases of hyperinsulinism, renal glycosuria, pregnancy and lactation. Four-fifths of all cases with hypoglycæmic symptoms fall into one of three main groups—hyperinsulinism of organic origin, functional hyperinsulinism and hepatic disease. For each of these three groups the treatment is different, so that it is essential to establish an accurate diagnosis at the outset. The clinical course in the organic hyperinsulinism and hepatic types is towards progression of symptoms, the attacks becoming more frequent and more severe. In the hepatic type there may be other symptoms suggestive of hepatic dysfunction, and the hypoglycæmic symptoms tend to come on in the early hours of the morning. Conn has found that the fasting pre-breakfast blood-sugar levels, the dextrose-tolerance test, and liver-function tests are of value in differential diagnosis. He considers the fasting blood-sugar data obtained after the patient has been on a restricted carbohydrate diet difficult to interpret, but a fasting pre-breakfast blood-sugar value of 50 mg. per 100 c.cm. in a person who has been on a normal diet affords strong diagnostic evidence of organic hypoglycæmia. Cases of functional hypoglycæmia—and this group provides the majority of clinical cases—are not associated with low fasting pre-breakfast blood-sugar levels. The factors influencing dextrose tolerance and the difficulty of interpreting hepatic function tests has led most British workers to be sceptical of data based on the interpretation of the latter, but Conn, with the majority of American workers, considers the tests to be of value, provided standard conditions are used.

The treatment of the functional hypoglycæmias is entirely medical. Conn advocates a diet high in protein (120–140 g. a day) and low in carbohydrates (50–75 g.) with fat sufficient to ensure an adequate calorie value. The rationale for such a diet is that at least half of the protein is utilised by the body as carbohydrates and that

1. Conn, J. W. *J. Amer. med. Ass.* 1940, **115**, 1669.

the comparative slowness of the breakdown of the protein molecules provides a small but continuous supply of carbohydrate. In the treatment of organic hyperinsulinism and hepatic hypoglycæmia surgery must be considered. After the report of a case of islet-cell tumour by R. M. Wilder and his co-workers,[2] numerous reports of laparotomy on supposed cases of hyperinsulinism have appeared, but only in about half of the cases has a pancreatic abnormality been discovered. Conn has therefore laid down what he considers to be the minimum conditions which must be fulfilled before a laparotomy is contemplated—absence of extrapancreatic causes of hypoglycæmia; abnormally low level of blood-sugar during the symptoms and the rapid relief of symptoms by administration of dextrose; repeated fasting blood-sugar values below 50 mg. per 100 c.cm. when the patient has been on an adequate diet; and depression of the fasting blood-sugar below 40 mg. by carbohydrate restriction. If these criteria are fulfilled in a patient past middle life with progressive symptoms a malignant condition is probable and an operation must not be delayed. The indications for operation in the hepatic group are more difficult to define. Conn cites a case of chronic cholangitis in which there was no clinical evidence of hepatic disease, and only full investigation of the hypoglycæmia revealed evidence of hepatic damage, yet this patient was completely cured by removal of the gall-bladder and biliary drainage. If there is any evidence of a degenerative or a destructive lesion of the liver treatment consists in the provision of a diet rich in carbohydrates, vitamin A and calcium, which is known to aid in the restoration of damaged liver cells.

Hypoglycæmia, then, is no longer a mere academic or diabetic problem, but must be considered a possible cause for syncope, altered mental states and atypical dyspepsia. Further, it affords a possible metabolic basis for a few more cases in that huge morass of clinical material all too readily classified as functional.

PSEUDOFRACTURES

MANY diseases affecting the skeletal system are complicated by fractures which are often multiple and symmetrical and occur spontaneously or after slight trauma. Among them are the varieties of osteogenesis imperfecta and the various types of osteomalacia. Such fractures are commonly only partial, without displacement of the fractured surfaces, and because of the underlying bone pathology their radiographic appearances differ from those of the ordinary traumatic fracture. These peculiarities have led several radiologists to express the belief that "pseudofractures" are a definite clinical entity and they have even been called Milkman's disease and other names after various workers who have reported examples. McCullough,[3] however, who has lately made a close study of them, concludes that there is no ground for the belief that pseudofractures represent a new disease. They are partial fractures produced by excessive strain on a diseased bone and there is recent confirmation of the original hypothesis of Looser that they begin as infractions of individual trabeculæ. Indeed, as in the well-known "March fracture," excessive strain on normal bone may lead to a similar type of fracture. Also such fractures have been produced experimentally by Sai. Radiographically pseudofractures assume three forms. In malacic diseases the lesions appear as small subperiosteal notches in the cortex or as irregularly circular areas of decalcification. Later this decalcification may extend across the bone to form a band ranging from a millimetre to more than a centimetre in width. At this stage, of course, gross trauma may readily convert the pseudofracture into a complete one. In cases not associated with osteomalacia the lesions may appear as cracks or fissures extending part way across the bone, and periosteal reaction is somtimes observed, especially on the concave side of pathologically curved bones, and the ends of the apparent fragments often show a marginal sclerosis. The third form is akin to March fracture in that there is fusiform callus formation and no fissure or band of decalcification can be detected. These changes are readily explained by trabecular infraction leading to partial fracture. McCullough compares the process to what happens in a piece of malleable metal when it is repeatedly bent back and forth. With slight movement the increase in local circulation produces local decalcification, and replacement of calcium is only accomplished if calcium is available for deposition. In one interesting case of multiple pseudofracture complicating osteogenesis imperfecta, reported by Macey,[4] it was noted that while there was no abnormality in serum calcium and phosphorus or in studies of calcium balance serum phosphates was absent, and after surgical treatment with consolidation of the fracture the serum phosphatase became normal.

2. *Ibid* 1927, **89**, 348.
3. McCullough, J. A. L. *Proc. Mayo Clin.* 1940, **15**, 785.

OIL IN THE LUNG

WE live in an uncertain world. Even liquid paraffin, long reputed blameless, has its sinister aspects. Its action on the peritoneum was described by A. H. Cruickshank[5] in our columns not long ago, and he mentioned briefly its effect on the lung. Cases of oil-aspiration pneumonia have been reported in America for several years and Freiman, Engelberg and Merrit[6] last year recorded a group of 47 cases of which 41 were chosen from among 3500 consecutive autopsies performed at the Montefiore Hospital in the past ten years. The patients ranged in age from 20 to 82, but as the hospital is for chronic cases most of them were elderly, and many were suffering from debilitating illnesses, associated in some with dysphagia. Oil had been taken in various ways: by mouth as an intestinal lubricant; intranasally as a spray or drops; and intratracheally as a lubricant for a tracheotomy tube. Analysing all cases reported as well as their own, these workers found that by far the commonest route was oral; out of 105 cases, 83 of which had come to post mortem, 49 took oil by mouth and 23 used it both orally and nasally. Various oils were implicated, but liquid paraffin was easily in the lead. In young children cod-liver oil and cream have occasionally produced the condition, but vegetable oils, such as iodised poppyseed oil used in bronchography, rarely give trouble; chaulmoogra oil is an exception to these. Liquid paraffin, being bland, can pass into the trachea from the pharynx without the patient realising it; it excites no cough and since it clogs the cilia is not removed again at once, but trickles to the lung bases under the action of gravity. The immediate response of the lung is to throw out macrophages which take up the oil, developing in the process a foamy appearance. Macroscopically the affected areas of lung are grey or yellow and moderately firm, protruding slightly above the level of the surrounding tissue. Gradually the patches become firmer and greyish-white, when they may be mistaken for tumour metastases. Later the lung becomes fibrotic and may finally produce masses of hyalinised fibrous tissue in which oil is entrapped—paraffinomas in fact. Various stages of the condition may be found in a single lung if the use of paraffin has been going on for years. The condition itself gives rise to no characteristic symptoms but in elderly people it seems to be sometimes associated with intermittent pulmonary infections, the episodes being accompanied by cough, fever and prostration. Radiography in the early stages shows increased markings in the lower lung fields. Later, shadows

4. Macey, H. B. *Ibid*, p. 789.
5. Jan. 4, 1941, p. 4.
6. Freiman, D. G., Engelberg, H. and Merrit, W. H. *Arch. intern. med.* 1940, **66**, 11.

representing areas of consolidation are formed in the bases, extending from the hilum to the diaphragm. The upper lobes are only affected late. The differential diagnosis is from bronchiectasis, unresolved pneumonia, pulmonary metastasis, tumour, infarct and tuberculosis. The writers consider that though the condition is commoner than is generally supposed, the administration of oil does not necessarily mean that oil aspiration will occur; liquid paraffin is taken by thousands with safety. It is as well to be on guard, however, and if the condition is suspected to stop the use of paraffin. In elderly, debilitated and especially dysphagic patients its use is not without danger, and its use for old recumbent patients, patients with chronic mental illness or mental defectives might well be discouraged.

WENCKEBACH

THE death of Karel Frederik Wenckebach breaks the last link with Vienna as an international centre of medical culture. Wenckebach succeeded to Carl v. Noorden's clinic in 1911 and became one of the most popular teachers in the university until he resigned his chair in 1929. But his link with this country was something apart. He was an honorary fellow (the last survivor) of the Royal College of Physicians of London; he delivered (and we had the privilege of publishing) the St. Cyres lecture on circulatory problems in beri-beri; and on his visits here he moved among friends who spoke of him among themselves as "Winkle." He was of course not German-born. His parents lived in The Hague. He qualified at Utrecht in 1888 with the intention of becoming a doctor in the fens. But the urge to find out how the human heart works got hold of him and he was called to the chair of medicine at Utrecht where he spent ten fruitful years working on the irregular heart. He reached Vienna via Strassburg, as it was then called. On his 75th birthday celebrated by his colleagues there two years ago it was emphasised that his power to win hearts was bound up with his love of nature and of art. He was in fact a good European.

RADIATION DOSAGE IN CERVICAL CARCINOMA

IN recent years there have been several attempts to arrive at the optimum dosage in the treatment of carcinoma of the uterine cervix by radiation. It is known that a small dose is of little value and that it is possible to do more harm than good by over-dosage. Miss Margaret Tod,[1] in the second of two papers, emphasises the importance of attempting to assess the "dose" at two selected points in the pelvis. The first, point A, is situated 2 cm. lateral to the central canal of the uterus and 2 cm. from the mucous membrane of the lateral fornix in the axis of the uterus, and lies at the base of the broad ligament. The second, point B, lies 5 cm. from the mid-line on the same level as point A, and is either in or near enough to the obturator node to give a measure of the dose received by it. These two points are the same distance from the cervical canal, though at a slightly different level from those selected by E. L. Frazell[2] in his attempt to correlate tumour dose and five-year survivals. From a study of some 370 cases of carcinoma of the cervix treated with γ rays, or with γ rays and X rays in addition, Miss Tod reaches some interesting conclusions. She has analysed the results according to whether the patient was treated with radium alone, and whether the exposure to radiation was continuous or divided, or whether X rays were used in addition. From the evidence obtained it appears that, allowing for inevitable inaccuracies in calculation, and for the variable reactions in different patients, it is possible to suggest doses to be used as a basis for future treatment. Thus Miss Tod suggests that when radium alone is used the maximum effective dose is 7500–8500 r in 6–7 days or 8500–9500 r for 3 or 4 serial weekly applications, and when X rays are employed in addition the summated dose should not exceed 9500–10,500 r at point A over a 4–6 weeks over-all time. She also points out the danger inherent in raising large volumes of tissue to a high dose. W. V. Mayneord[3] has recently calculated some total energy absorptions in X-ray and γ-ray treatments. The "integral dose" need no longer be regarded as a completely unknown quantity, and it would be interesting if Miss Tod could make this calculation for the various techniques employed so as to note the effects of irradiating increasing volumes of tissue quantitatively. She has done excellent work in suggesting optimum dosage levels for treatment at certain specified points, but to decide the most advantageous method to apply X or γ radiation it is necessary to determine not only the dose at certain points in the pelvis but also the complete distribution of the radiation in space. This has already been done for an X-ray technique,[4] and a paper by Professor Mayneord on the volume distribution due to a radium technique is in the press.

1. *Brit. J. Radiol.* January, 1941, p. 23.
2. *Amer. J. Roentgenol.* June, 1938, p. 861.

KNOWING AND LIVING

SCIENCE and social progress mould and direct each other, and though ignorance and vested interests baulk progress there has been in the last century a complete revolution in the transport of goods and ideas, the war against dirt, medicine, conditions of labour and the Englishman's home and his use of leisure. This is well shown in Mr. F. Sherwood Taylor's "The Century of Science 1840–1940" (Heinemann, p. 279, 8*s.* 6*d.*). In 1840 four families often lived in one room, twelve feet square, and notorious centres of squalor, such as London's Rookery of St. Giles and Frying Pan Alley, were common in every big city. The putresence of slums in the early nineteenth century with their smell of sludge and privy-midden is vividly described. Before the discovery of the processing of rubber, bottle-fed babies sucked real calf's teats preserved in spirit; and "pobs" or pieces of bread boiled into a watery paste were the staple diet of newly weaned north-country children. Dr. Taylor is quick to see the social significance of familiar things. The science of the moving picture has not only provided a characteristic occupation and a soother for the people, but for the first time in history it has given the mass of young men and women a place to sit together in winter. Medicine, he rightly thinks, could have done more by maintaining health rather than treating disease, and he makes a good point by saying that the yearly amount of money spent on medical research in this country is the same as was needed to kill 32 of the enemy in the last war. He goes on to note the effect of science on the evolution of the modern home and of clothing, and finally tries to show that the lack of respect for truth, in science as elsewhere, is the cause of present world unrest. In rejecting the spilth of many similar books Dr. Taylor has interpreted freshly the influence of science on the growing art of living.

Mr. MALCOLM MACDONALD will be missed at the Ministry of Health but we cannot grudge the transfer of his conciliatory and humanistic outlook to a sphere with greater freedom of opportunity. Mr. ERNEST BROWN takes up the portfolio with a fine experience of social problems and a recognised ability to deal with any situation which turns on the equitable distribution of resources. We can say hail and farewell in the same breath as hail and well met.

Dr. HAROLD SCURFIELD, who died at Letchworth last Saturday in his 78th year, was medical officer of health for Sheffield 1904–21 and held the university chair in public health. His knowledge of public health theory and practice was encyclopædic and for many years he contributed weekly to our columns.

We also announce with regret the death of Dr. WILLIAM BULLOCH, emeritus professor of bacteriology in the University of London at the London Hospital.

3. *Brit. J. Radiol.* July, 1940, p. 235. 4. *Ibid*, May, 1939, p. 281.

In England Now

A Running Commentary by Peripatetic Correspondents

"A FRANTIC monotony of disorder" is, I think, the phrase used by the Hammonds to describe the miles of jerry-built houses thrown up to house the working classes during the industrial revolution. It is a phrase which, in one mood, comes to mind after spending some months in visiting public air-raid shelters in London and the provinces. "Frantic" because even the least introspective must consider this a frantic world in which the lord of creation—not to speak of Mrs. Lord and the little Lords—must spend his nights in underground repositories designed only for bargains, wines, sewers or tube railways; "monotony" because, although each shelter is different from the next they are monotonously inadequate as dormitories ("Hygienically speaking," as Lord Horder has said, "there is no such thing as a good public shelter; only bad and less bad"); "disorder" because however clean, tidy, well canteened, be-closeted and aid-posted a shelter may be it necessarily has that temporary and disorderly air seen in a gipsy camp or in those collections of Hairy Ainus or Congo Pygmies one paid a shilling to see at international exhibitions in the dear dead days of peace. Yet in a less pessimistic mood the description is seen to be unreal, and would certainly be rejected by the shelterers themselves, most of whom, after all, have come from houses to which the phrase was originally applied. A party of American hygienists (loathsome but apparently necessary word) who went round some unselected shelters seem to have been chiefly impressed by the amount of work which has been and is being done in them for the sake of what is—as Sir Wilson Jameson has pointed out—only some 5% of the population, even in London. As they remarked on the expenditure of bricks and mortar, on closets, canteens and aid posts, I had to defend it by re-telling the story of the American military attaché at the Dardanelles, who, asked what he thought of our situation after the landing, replied "Waal, General, I guess you're between the Devil and the W.C." It is, therefore, somewhat unfortunate that, unlike the many "angels" who have not feared to tread the shelters since the earliest days—East End parsons, Quakers, Red Cross and St. John workers, doctors and municipal officials, ministers of the Crown—those that chiefly rushed into print seem either to have political axes to grind or wish to generalise from the particular as a result of a brief sight-seeing tour. Perhaps the authorities were slow in getting off the mark; perhaps the borough machinery failed always to stand the strain; perhaps in every shelter the medical supervision is not all it might be, but does that justify wasting paper now by describing the conditions of last November? Or saying that hardly any large shelters have canteens when the reverse is the truth? Or blackening the shelter medical service because it is not a complete state medical service for the nation?

* * *

Dr. Thomas Parran, surgeon-general of the United States, is honouring us with a visit and the Washington correspondent of the *Daily Telegraph* says that he wishes to study the hygienic measures we have taken in shelters because "American medical opinion is amazed at the way in which Britain has prevented epidemics." This amazement, if true, is perhaps a little premature,—"Beware the Ides of March"—and in any case modern epidemiological theory, having taken a nasty knock or two lately, is inclined to be more fatalistic than ever and would certainly not ascribe the absence of an epidemic to any feeble endeavours made by those responsible for the public health. Nevertheless I have little doubt that General Parran will be impressed with what has been done. To give some examples, major and minor; the prompt solution of the problem of sewage (disposal from tube platforms by blowing it up to sewer level with the compressed air of the signal system); the discovery and elimination of a species of mosquito found to be breeding all the year round in the underground railway system; the provision in every large shelter of a medical aid post, including a visiting doctor, a nurse, a sick bay, and a formidable equipment of drugs; the provision of a doctor for emergency calls to every public shelter; the building of water-closets on a large scale (96 with 60 feet of urinal in one shelter); masks, air sprays, delousing apparatus and extensive new powers to exclude from shelters, to examine children, to cleanse persons and bedding, and so on. We may feel about the lurking epidemics what the Scottish soldier said about his blankets after they had been treated for lice, "They're a' there yet!" But at least we can echo his friend's reply, "Aye, but they must have gotten an awfu' fricht!" According to report, Dr. Parran's party hopes to go on later to Paris and Berlin and they will have some interesting comparisons to make. Is it a question of "Oh, to be a neutral now that spring's there!" or do they expect Paris and Berlin to be in British hands by then?

* * *

The other day I had to perform a radical mastoid operation on a middle-aged man and decided that the cavity should be skin-grafted. I had had no occasion to examine his chest (a chore left to the houseman, whose opinion on such matters is probably of more value) or his legs, and when the thigh was exposed I was horrified to see an enormous tattooing of one Mary in an enticing state of déshabille. The nursing staff had "prepped" the area in the usual way and without comment had left it to me. We then uncovered the rest of the patient and found Anne on his other thigh, in an equally naughty pose. His chest, abdomen, back and upper arms were also covered with decorations of a more or less erotic nature. This once-prevalent custom among seafarers seems to be less popular nowadays. It is difficult to decide whether the underlying desire was to stimulate their own visual appreciation or that of others, or whether it was merely an "old Spanish custom." What with the complicated designs and the stoicism required to endure the pain inflicted in the process, the pictures must have been a source of much pride and prejudice. I was quite unable to decide whether tattooed skin could be grafted, and, if so, what would happen. Suppose I transferred some of Mary to the mastoid, would it have any influence on the man's mentality? Would it send him seeking Mary in whatever far-distant corner of the earth he had encountered her? Suppose he subsequently developed tinnitus, would voices whisper "Mary"? Would the skinned portion of Mary be replaced with an undecorated regrowth of his integument? Would I be liable for damages in this event? Perhaps, I thought, I had better telephone the Medical Defence Union first. Weakly, I sliced portions of normal skin from among Mary's sprawling limbs and left her intact.

* * *

Whenever I see that the Minister of Etcetera in the middle of a great war has found time to go and address a Rotifers' lunch or give away the prizes at a seminary, I wonder. Surely it would have been much better for his job if he'd gone for a nice country walk by himself and had a little of that quiet cogitation which is the very nursery of statesmanship. Why do they all do it? Well, I've had only one of this kind under close observation and there was no doubt why he did it. He enjoyed it; if he was away from the eyes of his fellow men he was unhappy; he liked to be with them in large numbers as the most prominent person among them; the cheers, the exaltation of his ego, the newspaper reports, the sense of being important, all this was the alkaloid that stimulated him to further efforts in the public cause, and the drug that gave him a craving for more. He would snatch at a chance of making a speech even at a Women's Institute meeting as avidly as a morphia addict if he can't get anything stronger will take to paregoric. Of course, he rationalised the process, as duty, or recreation, or keenness on that particular institution, or even cynically as pure vote-catching, but this deceived none of the inner circle. He dropped all pretence with his secretary and she caught it well and good if there were blank spaces in his engagement book. Sometimes I, who, he knew, had the appropriate receiving apparatus for that sort of thing, would hear an insincere voice, representing a small minority of his cortical cells, saying "Oh for the quiet of the country—away from all this," "Oh to be just Mr. Smith again." Then the telephone would ring and the reporters arrive, his eyes would brighten, his face would set in a peculiar way, minor manic qualities would

be released, and he would be quite a different person. Obviously there is a definite mechanism here, a mechanism that lures men with certain characteristics to become leaders, holds them in an addict's vice of adulation and publicity, extracts much valuable work from them, makes them sensitive to any draught of criticism. It gets every ounce out of a man as no payment or rationalised process could do, and at the same time keeps him controlled by those he leads, a strange device by which the slave is made to work hard in the galley, and love it.

* * *

Riding down to Cambridge in one of those snappy American ambulances that you see about, I learnt from the beautiful and talkative driver that the service is run by two Americans. They have some six hundred women drivers—not all American—who are paid £2 a week for billeting but otherwise work voluntarily. There are about half as many cars—Packards, Buicks, Chryslers, and others—all painted grey with a red stripe round them. There are also a number of ambulances and special vehicles, such as a dental travelling lab., fully fitted out from America. The cars are for the use of the E.M.S. but I believe expenses are paid from America and that the petrol comes over in special tankers. They are mostly used in transferring patients and occasionally doctors from one centre to another, and the girls have done some pretty good feats of driving. Different American townships have presented different things, and the dental workshop was presented by the dental surgeons of America. Altogether they are making a fine contribution to the war effort of which too little notice has been taken.

* * *

It seems ages since I huddled in a chair in front of the fire and knew that I was "for it." That hot spot in the throat was unmistakable, the railhead, the forward base from which the enemy was going to advance on a wide front. Talk about your modern three years or so of war—mine puts the Thirty Years' War to shame. Every winter, and perhaps oftener, the enemy has launched (and I suppose will go on launching) attacks of great nuisance value which force me to an inglorious strategic retreat. Upper respiratory infection, influenza, epidemic catarrh, call it what you will, it was on the move and I had better retire to my tents, O Israel. Now, have I got that quite right? Looking into the fire, no, drooping and gooping and mooping, signing the aching bakehouses, as you were, baking the aching sinuses, you see it was a Saturday and I was reading an appreciation of James Joyce in the *New Statesman*, I knew that I had got it the wrong way round. It had struck its tents, humanity was on the march, and I was on the move—and that turned out to be true about this attack, too, afterwards. My wife said, "What's the matter bad luck darling I hope to goodness you don't give it me go and get into bed I'll put a hot bottle in where's the thermometer O Lord it's up to 102 it will mean that you're in bed for at least a week well if Hitler comes you'll jolly well stay there no cold cellar for you to catch pneumonia in I don't think I should have a hot bath in case there's an air raid dear." To which I replied "O blast, O blast, O BLAST," looked into the medicine cupboard on my way up, and could find nothing suitable to my condition, as nobody has sent me any samples for a long time. And so to bed, and my wife asking me if there is anything more she can get me, and I replying that all I want is a large supply of cold water and to be left alone (I did not add "to die in peace," for that would have been not quite sincere; I felt like that only part of the time).

Scene II.—A few days later. On a table by the bedside, on the floor, even on the bed itself, are books, gradually accumulated by request of the invalid. You see, as soon as I know that I must perforce retire from the world for a season I become all penitence and good resolutions. So many books on my shelves have been there for years, and I ought to have read them long ago, but the cares of this world, a lack of intellectual discipline, laziness, wrong moods, iniquity of some sort or another, have let them go unread. My wife had originally, off her own bat, brought me the month's *La France Libre*, her own thriller from the library, and my copy of the *Lancet*. Sometime I would read them; but with the prospect of at least a week indoors, the immediate need was thought; deep, serious, well-pondered and balanced thought. In the intervals of being ill, and during convalescence, what should I do? Write about shop, or outside medicine? I thought not, for it is such a fag to manipulate a pencil or pen in bed, especially if you do not want to sit up. Read? Not shop, at any rate; let us have a change and enjoy stolen sweets. What better than make up for lost time, and get the dust blown off some of the neglected shelf-dwellers? What about the Nonesuch edition of Rawlinson's translation of Herodotus which I have only glanced at during our five years cohabitation? A day of fitful, semicomatose and perspiring thought under the bedclothes produced the important decision that the book was altogether too big and heavy for a febrile invalid; nevertheless the shadowy recollections of the actual volume itself, woven into dreamy and inconsequential thought about this vital matter, left me with an almost voluptuous sense of duty nobly and highly done (evening temperature 101° F.). So as the days went by and the pyrexia subsided piles of books gradually invaded the bedroom. This is the list today, when I am up again, and returning most of them to their shelves, still unread: "The Development of Modern France," by D. W. Brogan; the old leather-bound copy, which I got in a little Surrey secondhand furniture shop for ninepence, of Samuel Johnson's "Prayers and Meditations"; Collingwood and Myres' "Roman Britain and the English Settlements"; some philosophy of Maritain and theology of John Oman; the book of the Linguaphone German course, and one or two simple German readers (having started to learn German already about a dozen times, and getting "just so far," shall I start again in real earnest?); the first volume of Toynbee's "The Study of History"; Blunden's "The Face of England," and also "Nature in English Literature" (on the inside page of which he wrote and *Amen*-ed, years ago, James Thomson's couplet "I care not, Fortune, what you me deny, You cannot shut the windows of the sky"); the first volume in the 1799 edition of Sewel's "History of the People called Quakers."

In the whole fortnight I have read—Oh the things, that we ought to have done and have not done, and the things we have done that we ought not to have done!—the two morning papers each day and done occasional bits of the crossword; a couple of paper-backed thrillers which were already lying about; the *New Statesman*, and *Time and Tide*; the contents page and one or two other pages of the *Lancet* and the *B.M.J.*; "Waverley"; and "Peveril of the Peak." The latter proved itself an admirable bedbook—at least my copy did, for each of the four volumes was so small and easy to handle, the print so good, that it could be read comfortably with all but one's nose and thumb inside the bedclothes. I must claim also that at least I said "how do" to most of the others, dipped into them, smelt their backs, noted their pagination; for some of them, indeed, this is not their first friendly, though vain, sharing of my influenzal retreat. I shall read them all, one day—perhaps. I should like to, anyhow.

I must confess to having looked at one or two medical books, also, reading a chapter or two here, looking up a special subject there. More than ever I realised how few modern medical books read easily; so many are moderately worthy, but dull and lifeless. I was so depressed with the two which I consulted that I took a corrective dose of Trousseau's wine (literary, not pharmacopœial) from one of the volumes of his "Clinical Lectures." Perhaps the *Lancet* leader-writer is correct in assuming that most modern medical textbooks are written by registrars with their way to make; and even when the writers have made their way, so many are still registrars who have never grown up.

* * *

An hour or two after I had read your peripatetic's note on Gilbert White's summary of the weather between 1768 and 1792, I started on J. W. Fortescue's introduction to the "Memoirs of Sergeant Bourgogne (1812–1813)." He finds something of a parallel to Napoleon's retreat from Moscow in our own military history. "We too have had our disastrous retreats, though we may not know very much about them. The worst was from Holland to the Ems during the very severe winter of 1794–95. Two-thirds of the army

perished, and if the retreat had lasted for but three days more hardly a man would have survived. . . . For some days food was scarce, but drink was obtainable, and the British fought pitched battles for it against their Hessian allies. At the end of one day's march a party held a carousal round a cask of spirits, and were all found round it on the next morning, frozen to death. And once again there were women in the retreat; and the sole narrator records that he saw a mother frozen to death with her baby in her arms, and the milk frozen hard on the dead baby's lips."

* * *

Now that housewives have got to make the best of the foods they can get, I hope to put into practice an idea I have had for seven years. Take a couple of large floury potatoes and bake them; mix a wineglassful of red wine with some well-reduced meat stock; fill a hypodermic syringe with this and inject it into the potatoes. What a pleasant surprise for your guests who thought they were only going to get a plain baked potato. The contents of the syringe can be varied. Put in white wine and you have pommes piquées au vin blanc. A little tomato juice: pommes piquées au jus de tomates. A little celery seed (Cerebos sell it) and you have celery potatoes. I am sure it would work. The other thing I urge is that people should grow more cardoons, a giant thistle much the same as the globe artichoke, but eaten more like celery. They are delicious vegetables with a flavour slightly less pronounced than that of celery, but stronger than that of a leek. They should be served with a mild cheese sauce.

* * *

As the deafening report of the explosion died away the air-raid warden said, "Come on, Doctor, let's go and have a look." In the fading light of a December afternoon we emerged from the house and made our way towards the column of smoke and dust that was still visible among the scattered suburban houses about 200 yards away. The destructive effects of the bomb were remarkably circumscribed; there was an open space covered with rubble where a few minutes earlier had stood two highly desirable, semi-detached modern villas, happily untenanted. There seemed to be nothing for either of us to do, and as the sound of the planes had not ceased we agreed that we had better return to the shelter. Just then, however, our attention was attracted by high-pitched shrieks which seemed to come from a distance. "Children?" queried the warden. "No," I returned, "those aren't children's voices; but I can't say what they are." "Where is the noise coming from?" asked the warden, increasingly mystified, as he peered into the gloom. No answer from me was necessary, for at that moment half a dozen hens in a state of great agitation came fluttering down on us from the sky. They had evidently been caught by the blast of the high-explosive bomb, and were but then returning from their journey to the stratosphere. For a moment after they landed they trod the ground somewhat gingerly, but soon they were wholly absorbed in the business of foraging among the debris, apparently oblivious of their grotesque appearance, for they had been almost completely defeathered in their meteoric flight.

* * *

I have often wondered whether London's legion of pigeons should not be trapped and sold for the Red Cross. According to me, they ought to bring in £25,000. And after all pigeons are vermin; they destroy crops and they are much nicer to eat than the bird that is the great pest in Australia—the common sparrow. The sparrows there came originally from England; some fool took a couple out and they bred in record time. Soon half of Australia was covered with them, but fortunately Perth and all the district around was free, for that is one of the biggest fruit-farming areas in the world. One day it was reported that two English sparrows had been seen in the public park in Perth; it seems some super fool had brought a couple along with him two thousand miles from the other side of Australia. There was a frantic to do; everyone in Perth depended on the prosperity of the fruit farmers for a living. Every school in the place was given a half holiday and the children rushed off to catch the sparrows. The fire brigade was called out, and £5 was offered for the capture of each one. When they were caught the town sighed with relief.

Special Articles

MEDICINE AND THE LAW

The Nurse-Anæsthetist

WE noted last year a protest against the proposal to employ a "nurse-anæsthetist" at a hospital (see *Lancet*, 1940, **2**, 307). Mention was then made of legal restrictions on such employment in Canada. The *British Journal of Anæsthesia* (1939, **16**, 142) had given its readers an account of the Canadian case of McFall *v.* Victoria Hospital and Turner, from which we are permitted to quote.

McFall was a workman who met with an accident necessitating operation. Dr. Turner performed the operation at the defendant hospital, the anæsthetic being given by a nurse-anæsthetist. McFall died during the operation; his widow sued the hospital and the surgeon in the Superior Court at Montreal. The deceased was said to have been a difficult subject for a general anæsthetic; he suffered from alcoholic excess and abnormal blood-pressure and there was a fatty accumulation around the heart. The court thought that an anæsthetic should not be administered to such a patient by anyone not medically qualified. In such a case the defendants should have been doubly prudent; the patient should have had the increased protection of a specialist in anæsthesia; McFall having chosen to undergo the operation, it became the duty of the surgeon, in view of the inherent dangers of the anæsthetic and the particular risk to this patient, to choose and, if need be, to insist upon a first-class anæsthetist capable of meeting any complications which might occur. The employment of a general anæsthetic being a dangerous act, it followed that it constituted a fault in itself to propose for this duty a young nurse who had little of the medical education of a physician. The specialist can note the signs of the patient's reflexes, pulse, breathing and colour; he can detect a sudden complication and act quickly, doing what is required and nothing else. The defendants were not entitled to say that the surgeon was available to deal with complications of anæsthesia; the surgeon must concentrate upon the operation itself; he should not supervise the anæsthesia. As the court could not determine the exact cause of death, it could not attribute blame to the nurse-anæsthetist. It could not decide that McFall would have still been alive if a properly qualified anæsthetist had been there instead of the unqualified nurse. There was no proof that the death was due to her inexperience or incompetence.

It would be interesting to have the verdict of an English coroner on facts similar to those in McFall's case. In England the issue of negligence would, as usual, depend on the decision made by judge or jury on a particular set of facts in the light of expert medical or surgical evidence. If we are to contemplate the possible liability of a surgeon in England who found himself, like Dr. Turner, operating on a patient to whom a nurse-anæsthetist is administering the anæsthetic, the same question would arise as in the cases where a nurse is said to be at fault in counting swabs or in burning a patient with a hot-water bottle. Plaintiffs have tried to fix the surgeon with responsibility for the nurse's acts of omission in such cases. The surgeon usually replies that the nurse is specially trained for these duties and acts independently of him when carrying them out. It is a question whether she is or is not his servant or agent. In England we still await an authoritative pronouncement on this point. In an American work on "The Röntgenologist in Court" (1937) reference is made to a case (Emerson *v.* Chapman) where the Supreme Court of Oklahoma said that it was the defendant's duty "in using the nurses furnished by the hospital, to see that every act necessary for the operation under his immediate supervision and control was properly performed." If the nurse concerned, said the court, was not under his direction and control, he was not liable for her acts; the court held that she was. It by no means follows that our own courts would come to the same conclusion of fact.

Hospital's Liability for Nurse

Hospitals, as well as surgeons, are concerned in the question of liability for a nurse's negligence. An article on this topic by Mr. F. W. MacLeod is printed in the

December *Canadian Bar Review*. The Supreme Court of Canada, it seems, accepted in Nyberg *v.* Provost Municipal Hospital Board (1927) the dictum of Kennedy L. J. in the well-known case of Hillyer *v.* St. Bartholomew's Hospital (1909) that a hospital "is liable for the negligence of even duly qualified nurses employed by it in the performance of all duties other than those done under the direct orders of a physician or surgeon in the course of an operation." Less consonant with the decisions of the English courts is the proposition which Mr. MacLeod extracts from certain Canadian cases (in particular Sisters of St. Joseph *v.* Fleming, 1938) "there is no legal distinction per se between routine acts of nurses and acts requiring professional skill." Canadian and English law agree that the test of the liability is "whether or not the relationship of master and servant existed between the hospital and nurse at the time the negligence complained of occurred." Mr. MacLeod, however, quotes Davis J. as saying (in the last-named case) that there might be quite exceptional cases where other considerations would arise. Both in England and Canada it is clear that the hospital is not liable where the doctor has control. This raises a question of fact which is particularly interesting when the doctor is absent and the nurse is carrying out his instruction. In Vuchar *v.* Trustees of Toronto General Hospital (1937) the defendant hospital was held not liable where the doctor gave an express order "to use the electric cradle continuously" and the nurse applied too much heat and so burned the patient. Mr. MacLeod dismisses the idea to which Prof. A. L. Goodhart of Oxford University has given his support that the hospital might have a liability when the nurse is carrying out the instructions of a third party.

SCOTLAND

SCOTTISH STUDENTS' HEALTH

WE mentioned last week in our news column that the annual convention of the Scottish National Union of Students, held in Aberdeen, had given its approval to a scheme for setting up a limited panel system of medical insurance for students. Under this system, an attempt would be made to form a small medical panel in each university town, composed of a few of the younger university teachers, who would be invited to coöperate. They would be carefully informed as to the modest financial emolument involved. Students in each town would be asked to register their names at the local Students Representative Council office and pay a fee of, say, 10*s.* 6*d.* or £1. They would then choose from the panel the name of the doctor of their preference, to whom would be sent the students' names and addresses, with index cards on which essential data regarding any illnesses would be written, and the registration fees after a small deduction for administrative expenses. The registered student would then be entitled to call in this practitioner when he was ill. It was realised that the student response would probably be slow in developing, for few students were provident enough to think in terms of possible ill health, and fewer still thought of providing against such an event. At first, therefore, only a small panel would be needed, which could later be increased, on a basis of about 100 students to each doctor.

The suggestion to establish a Scottish student health insurance system arose because of an investigation by the national executive committee of the union into the existing health services, which revealed one notable deficiency. The healthy student in each university was offered facilities for free medical examination at which organic disease could be excluded and the grade of his physique recorded, and the desperately ill student or the student in need of an operation could receive free hospital treatment either in the general hospital wards, as in Glasgow, Aberdeen, and St. Andrews, or in a special students' ward, as in Edinburgh. There was, however, no special provision for the student who was ill in his lodgings—the one suffering from one of the minor maladies which, though not necessarily dangerous, might nevertheless be damaging to efficiency; or the student in the early stages of serious disease. At present the average student who fell ill in his lodgings was at a double disadvantage. He did not know where to apply for medical attention, because he was ignorant about the local medical practitioners, and he was haunted by the possible expense involved in calling in some strange doctor. As a result he often did not call in any medical help at all, or if he did he waited until he had become dangerously ill. It was to bridge this gap between medical examination of the healthy and hospital treatment for the very ill that the health insurance scheme was suggested.

GLASGOW WESTERN INFIRMARY

Sir George A. Mitchell, chairman of the board of managers of the Western Infirmary, indicated at a recent meeting that preliminary steps were being taken towards establishing an organised orthopædic service for the West of Scotland. The large general hospitals and the local authorities were already providing for a large number of cases, but there was still a lack of provision for the treatment of long-term cases. The proposal was to set up an organisation to coördinate all existing services and provide additional services as required. It had been initiated by the Central Council for the Care of Cripples in connexion with a fund of £70,000 which had been allocated to Scotland from Lord Nuffield's trust. There was need of a hospital in the country for prolonged inpatient treatment under open-air conditions, for additional clinics for outpatients, and for a service for the vocational training of cripples and placing them in employment.

A HUNDRED DENTISTS AND A'

Glasgow dentists have established a unique A.R.P. service which other areas might copy. There is a large first-aid post in the Town Hall, which is situated in the centre of the city. The building is close to a most congested area, where casualties might be high, and from which it is difficult to recruit intelligent part-time workers. Medical and nursing attention present no difficulties by day, for a staff of doctors and nurses is always available during office hours, but is not so easy to arrange at night. A large group of Glasgow dentists have therefore taken over responsibility for the post at night. Their training began with courses in first-aid, anti-gas work, and A.R.P. organisation. A hundred dentists attended, and of these more than half are now sleeping at the post, doing one night in eight with 7 on duty at a time. The sleeping quarters are not sumptuous but are comfortable, and part of each evening is spent in further training.

Parliament

ALTHOUGH the greater part of the parliamentary week in the Commons was taken up by a minute examination in committee of the intricacies of the War Damage Bill, the few hours occupied in the discussion of two votes of credit for the immense total of £1,600,000,000 overshadowed everything else. Members are becoming accustomed nowadays to periodical demands from the Chancellor of the Exchequer for grants of money for the prosecution of the war, the proportions of which are truly staggering judged by peace-time standards. But in spite of that, there was no-one who did not catch his breath when Sir Kingsley Wood announced that our daily rate of expenditure, which a year ago was £5,000,000, is now more than doubled. Our total national expenditure is now approximately £12,250,000 a day, since apart from war the other multifarious services of the state, including the social services, have to be paid for. It is a little difficult to grasp the significance of the fact that we are now spending at the rate of more than £4,000,000,000 a year, a figure impressive enough in itself, but all the more so when it is compared with the largest sum actually spent in any year in the last war—£2,432,000,000 in 1917. Nor did the Chancellor give the House any hope that we had yet reached the peak; on the contrary, he warned the nation that great as are our present burdens and sacrifices they must be followed by still bigger ones as our war effort rises to its tremendous climax. Civilian consumption must continue to be curtailed and the figures of saving as a result of the National Savings Movement, satisfactory as they are, must be exceeded. While in the view of the Chancellor of the Exchequer the danger of the so-called gap between taxation and saving, on the one hand, and expenditure on the other has been

exaggerated, he did not deny that there was a danger that prices may rise to excessive levels. He assured the House, however, that the Government were fully alive to this menace and would not hesitate to tackle it should the necessity arise. Such criticism as was offered by members of all parties was not directed to the size of the votes; everyone was conscious of the universal desire to speed up the national war effort to the greatest possible extent, and that astronomical figures of production cannot be expected in this most costly of all wars without corresponding figures of expenditure. There was a general demand that the sacrifices of the war should be spread over all classes of the community, but Sir John Wardlaw-Milne and others uttered a warning that this must not be done at the expense of national nutrition, and they pleaded that social justice should be done by some system of family allowances.

Medicine a Business

In the course of the debate on the committee stage of the War Damage Bill in the House of Commons Sir FRANCIS FREMANTLE raised a point of some interest to the medical profession. Clause 42 deals with insurance schemes and Sir Francis moved an amendment to make it clear that the word "business" used in the clause includes any trade, profession, employment, or vocation. He said that it was thought by the medical profession, for whom he spoke, that it would be best to use the interpretation of the word business, which is used in the Income Tax Act. He was not wedded to the exact wording so long as medical men were included. He understood that it had been said in the memorandum to this bill that the word business did include the professions; but he pointed out that there was nothing in the bill to say so, and medical men did not desire to trust simply to a statement of that sort.—Mr. LYTTELTON, President of the Board of Trade, said he was advised that the word business covered the professions, and that it would be dangerous from the legal point of view to insert the words proposed by Sir Francis Fremantle. At the same time there was something to be said for making clear to the ordinary reader the extent to which the word business applied. He did not know whether that could be done, but he promised to look into the matter. On this undertaking Sir Francis Fremantle withdrew his amendment.

QUESTION TIME

Medical Services

Mr. G. MANDER asked the Minister of Health whether, in view of the widespread dissatisfaction at present existing in the medical profession with regard to the failure to utilise to the fullest extent the services of the medical profession in the national effort, owing to lack of coördination and coöperation between the Emergency Medical Service, the medical services of the armed forces and the general body of civilian medical practitioners, he would consider the advisability of appointing a small non-medical committee to investigate the most effective organisation for utilising to the best advantage the medical services of the country.—Mr. M. MACDONALD replied: The Service Ministers, the Secretary of State for Scotland and I are not aware of any widespread dissatisfaction, but we have recently had the advice of a committee appointed to consider the steps necessary to secure a proper allocation of the available medical man-power between civilian and military services. The committee consisted of Sir Arthur Robinson, as chairman, and three medical men with wide experience of the various branches of the profession—namely, Sir John Fraser, Sir Kaye le Fleming and Professor Picken. Their report is now receiving our active consideration.

Rehabilitation of Blinded Civilians

In reply to a question Mr. MACDONALD said: Up to date 28 civilians (19 men and 9 women) have been reported to me as being in hospital with injuries resulting or likely to result in blindness. The records in the ministry do not show if any of these are under 16 years of age. Eleven of these 28 are already at St. Dunstan's. At present, the names of all such casualties who are not transferred to St. Dunstan's are being reported to the National Institute for the Blind, who are making provisional arrangements for their rehabilitation and for notification to local authorities; and arrangements to deal with larger numbers, if necessary, are under consideration in consultation with the appropriate agencies. The question of vocational training for a fresh occupation is the concern of the Minister of Labour and National Service, with whom I am in communication on the matter. Payment is made to any hospital in which a civilian blinded as a result of enemy action receives hospital treatment.

Hospital in Glamorgan

Sir WILLIAM JENKINS asked the Minister if he was aware that there were thousands of pounds of material lying waste at the Church Village Hospital, Glamorgan, and the essential timber for roofing was not supplied, priority claims promised, which had been made at intervals since January, 1940, were not fulfilled; would he take immediate steps to remove the obstacles so that the materials on the site might be used, as skilled workers were leaving regularly and the hospital was urgently needed for military and local purposes.—Mr. MACDONALD replied: One of my senior technical officers visited the site at the end of November and has recently conferred with the architect responsible for the work. A high priority has been given to the scheme and arrangements made which should result in rapid progress.

Accidents in Mines

In reply to a question to the Secretary for Mines Mr. DAVID GRENFELL replied: Provisional figures for 1940 show 910 persons were killed and 3186 seriously injured by accidents at mines under the Coal Mines Act. The figures for 1939 are 783 killed and 3155 seriously injured, and for 1938, 858 killed and 3157 seriously injured.

Public Health

Ireland: The Public Health

THE annual report of the Department of Local Government and Public Health for the year ended March 31, 1939, has recently been issued. It is unfortunate, if inevitable in present circumstances, that the report does not appear more promptly. This department seems to be the maid-of-all-work of public administration in Ireland and the report deals with a great variety of topics, ranging from such elections as those of the President of Eire and of the members of the Dáil and Senate to housing and the control of infectious diseases, the administration of the sweepstake funds and the dispensary medical service. The work of national health insurance, although under the supervision of the department, is dealt with in a separate report. The total amount received by the Hospitals Trust Fund from sweepstakes in 1938 was £1,386,158, out of which grants amounting to £570,909 were made to hospitals and nursing institutions, £107,935 of this being in respect of working deficits in the expenses of existing hospitals. A grant of £12,500 was made to the Medical Research Council, and one of £6104 to the Hospital Library Council, which was established during the year and is doing excellent work in the distribution of books to the voluntary hospitals and the tuberculosis sanatoriums. The total amounts paid out of sweepstake funds to voluntary hospitals or other voluntary organisations up to March, 1939, was £3,681,170, and to local authorities for hospital purposes £2,156,058. The amount standing to the credit of the Hospitals Trust Fund in December, 1938, was just over £8,000,000.

As regards the incidence of infectious diseases, there was a decrease in notifications from 8677 in the previous year to 8065. This fall affected nearly all the principal diseases, with the exception of diphtheria which showed an increase from 2511 to 2983 cases. The department has up to the present failed to establish an adequate scheme of immunisation against this disease. There has been a considerable fall in the mortality from tuberculosis in recent years, and the year under review showed the lowest rate yet recorded—1·09 per 1000 of the population. This is a reduction of 61% on the rate recorded in 1904. The highest rates recorded in 1938 were in the cities of Dublin and Cork, and the lowest in the counties of Longford, Leitrim and Roscommon. No substantial alteration occurred in the mortality from puerperal sepsis and accidents of childbirth in the decade 1927–36, but there has been some improvement in more recent years, probably due to the adoption of the newer chemotherapeutic measures. Infant mortality has shown some improvement, the rate being 67 per 1000 births in 1938 as compared with 74 and 73 in the two

preceding areas. The rates are still unduly high in some districts, particularly in the cities of Dublin and Waterford where the figures were 96 and 99 respectively. A recent survey of conditions in Dublin showed that 60% of Dublin mothers of the working class were unable to breast-feed their children. Free milk schemes and maternity and child-welfare schemes are in existence in several areas, but there are still many areas untouched. The report gives information concerning the regulations governing the production and sale of milk, but we learn little of how the system of administration works. The regulations apply only to the sale of whole milk intended for human consumption, and do not affect the sale of skimmed or separated milk, cream, or buttermilk. This is a serious drawback to the system, for separated milk is frequently used as a food both for human beings and for animals and has carried diseases to both classes.

The report gives figures for the number of patients attended and work performed under the poor-law dispensary system. The total number of new patients attended was 893,600, of whom 157,711 were attended at their homes and the remainder at the dispensaries. The number of vaccinations performed was 31,717, representing 55·7% of the births registered.

Infectious Disease in England and Wales

WEEK ENDED JAN. 25

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1302; whooping-cough, 2892; diphtheria, 1134; enteric fever, 11; measles (excluding rubella), 14,630; pneumonia (primary or influenzal), 1573; puerperal pyrexia, 156; cerebrospinal fever, 303; poliomyelitis, 5; polio-encephalitis, 1; encephalitis lethargica, 5*; dysentery, 63; ophthalmia neonatorum, 42. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on Jan. 31 was 2219, including: scarlet fever, 292; diphtheria, 315; measles, 859; whooping-cough, 163; enteritis, 24; chicken-pox, 211; erysipelas, 52; mumps, 10; poliomyelitis, 2; dysentery, 45; cerebrospinal fever, 57; puerperal sepsis, 7; enteric fevers, 6; german measles, 5; other diseases (non-infectious), 89; not yet diagnosed, 82.

Deaths.—In 126 great towns there was no death from smallpox, 2 (2) from enteric fever, 2 (0) from scarlet fever, 31 (1) from whooping-cough, 23 (3) from measles, 42 (1) from diphtheria, 44 (7) from diarrhœa and enteritis under 2 years, and 120 (22) from influenza. The figures in parentheses are those for London itself.

Fatal cases of diphtheria were scattered over twenty-nine great towns, Liverpool reporting 7, Birkenhead and Birmingham each 3. There were 8 deaths from whooping-cough at Birmingham. Blackpool reported 9 deaths from influenza, Birmingham 6, and Liverpool 5.

The number of stillbirths notified during the week was 195 (corresponding to a rate of 39 per thousand total births), including 9 in London.

Incidence of Influenza

During January the deaths from influenza in the 126 great towns have risen from 53 (8) in the week ended Jan. 4, to 69 (9) on Jan. 11, 99 (17) on Jan. 18, 120 (22) on Jan. 25, and 176 (45) on Feb. 1.

The returns of influenza deaths for the great towns, 176, almost precisely repeats the figures for 1929 (99, 122, 179). At first sight this is ominous for in 1929 influenza became very severe. But in that year 99 was reached a fortnight earlier and time is an important element; in general, the later a recrudescence begins the less likely is it to reach severe proportions. The most recent returns for London show a reduction in the numbers of daily admissions of influenza, bronchitis and pneumonia cases to hospital. It now appears probable that there will not be a sudden great rise in influenza deaths but mortality is likely to continue to increase. The age-distribution of the deaths is of the normal type, 56% are at ages over 65 and only 5% at ages under 25.

Return of Births, Marriages and Deaths

The quarterly return of births, marriages and deaths for the thirteen weeks ended June 30, 1940, issued by the Registrar-General shows an increase in births and marriages in England and Wales. The number of live births was 166,537, an increase of 2231 over the June quarter of 1939. Add to the figure of 154,336 births for the first quarter, it makes the total of births for the first half of the year 320,873, which is the highest total for this period since 1931.

The birth-rate per 1000 of the population was 16·2, and there were 48,482 more births registered than deaths. The corresponding increase in the second quarter of 1939 was 43,777. There were 116,134 marriages in the second quarter of 1940, which is an increase of 13,318 over the corresponding period of 1939. The marriage-rate per 1000 of the population was 22·5, which is the highest recorded in the June quarter since 1920. The number of civilian deaths registered in the second quarter of 1940 was 118,055. This was 86,294 below the total for the first three months of the year, and 2474 fewer than in the corresponding quarter of 1939. The death-rate per 1000 of the population was 11·8, compared with 20·3 for the first quarter of the year and 11·7 for the second quarter of 1939.

* In the return for the week ended Dec. 21 the number of notifications of this disease was incorrectly given (see *Lancet*, Jan. 25, p. 127). The figure should have been 3, none of which occurred at Colchester. In the same week there were 165 notifications of dysentery.

Letters to the Editor

ANÆSTHESIA IN THE SHOCKED PATIENT

SIR,—The question of choice of anæsthetic for the shocked patient which was the subject of one of your recent leaders and of a discussion in your correspondence columns is an extremely important one in these days of mass mutilation, because the chances of survival of severely shocked victims may be enhanced considerably by a wise and proper choice whereas an inappropriate choice may well be the factor which determines a fatal issue. This, of course, is no new problem for the surgeon or anæsthetist. In all urgent surgery in peace-time just as much as in war-time the selection of the anæsthetic and its management in cases of severe physical injury or other shock-producing conditions is the first and greatest problem which confronts the surgeon and anæsthetist as close collaborating partners in a team. In discussing this problem one cannot emphasise too strongly the vital importance of team-work when shocked patients are being dealt with.

The surgeon is fully aware of the greatly increased risk which attends operative intervention on severely shocked subjects and does everything possible to reduce such risk by instituting anti-shock measures and delaying operation, unless the urgency is extreme, until the patient's condition has improved to the optimum extent which his injuries will allow. The anæsthetist's responsibility to the patient and to the surgeon is a serious one. While anti-shock treatment will improve the patient's condition, the anæsthetist must always have in mind the fact that any necessary operative procedure will tend to nullify temporarily this improvement and he must consider his choice of anæsthetic with regard to that probability. He must choose therefore an agent which as far as possible will not, because of its toxicity or mode of action, contribute to the shocked state.

Furthermore, his part in the team-work is to help minimise the additional shock which may supervene during operation and which is due to sensory stimuli from the operation field, hæmorrhage, loss of body heat and fluids, and deficient oxygenation due to the recumbent position. Some method of nerve block is a positive way of interrupting the passage of shock-producing sensory stimuli and the claims of the protagonists of local infiltration analgesia and of regional nerve block regarding the advantages of such methods can be accepted with confidence. Their scope is limited however in urgent traumatic surgery where frequently the injuries are multiple and extensive. In cases where local analgesia is feasible but a marked degree of shock is present it is advisable to keep the patient asleep under light nitrous oxide and oxygen anæsthesia. This eliminates psychic trauma and reacts, beneficially on certain of the shock-producing factors mentioned above, such as loss of body heat and impaired oxygenation. In passing it may be noted that many surgeons appear much more at their ease when operating on the unconscious patient.

All things considered, most features of the state of shock indicate that the anæsthetic should be a light

inhalational one. Wherever possible toxic drugs such as chloroform and ether must be avoided because the presence of such agents in the tissues interferes with oxidation. Owing to their depressant effect on the respiratory and circulatory centres, and by virtue of their lipoid solubility which hinders efficient gaseous exchange, they increase the tissue asphyxia already present in the severely shocked patient. Fortunately, it is one of nature's compensations that such a patient is much less sensitive to pain and consequently anæsthesia is attainable by the use of less toxic agents. By using nitrous oxide gas and oxygen in a semi-closed apparatus such as the Boyle, anæsthesia can be maintained while at the same time factors such as low blood-pressure, cyanosis and deficient oxygenation due to hypostasis may be mitigated. The circulation is supported and the blood-pressure raised by the increased respiratory excursion and fuller expansion of the lungs which occurs in gas-and-oxygen anæsthesia. It is a fairly constant observation that the shocked patient looks better once he is under the influence of this combination. A certain amount of conservation of body heat and water vapour is possible when gas and oxygen are administered by a semi-closed method and this may be accomplished still more effectively if a closed circuit (CO_2 absorption) apparatus is used. If the anæsthesia is insufficient, as for example it might be for an abdominal section, the safest supplementation is by local infiltration or regional nerve block. A useful alternative, where local analgesia is unsuitable, is to add a little cyclopropane to the nitrous oxide and oxygen mixture until the necessary depth of anæsthesia is attained. This agent, in the hands of one accustomed to its use, is safe and suitable for shocked patients.

In conclusion, mention ought to be made of spinal-block analgesia. When severe shock is present this method ought not to be used. When, however, the degree of shock is moderate and the blood-pressure is not below 100 mm. Hg low spinal block is justifiable, but only for operations below the level of the umbilicus. Injuries of the lower limb such as fractured femur may be very satisfactorily dealt with under low spinal block induced with (say) 100–120 mg. of procaine. Hyperbaric solutions are safer and preferable to light solutions for such cases.

Edinburgh 12. JOHN GILLIES.

GLANDULAR FEVER

SIR,—Dr. Fuller in his article of Jan. 18 raises the question whether the Paul-Bunnell test is always positive in glandular fever. So far as one test or two tests at short intervals are concerned, I can say definitely that it is not, since I have seen a negative reaction become positive at a subsequent test. In the prolonged febrile type, in which the glandular enlargement is less marked and the constitutional symptoms more severe, I have known the reaction become positive for the first time during a relapse. Nevertheless one should always consider the diagnosis carefully if the reaction is negative even on one occasion, and it must be very rare for it to be twice completely negative. Dr. Fuller's cases are consistent with glandular fever in all other respects.

In your annotation you suggest that the negative reactions may be due to treatment with diphtheria antitoxin and sulphonamides, but I have on several occasions known the Paul-Bunnell reaction to be positive after administration of antitoxin or sulphanilamide. As to whether a virus other than that of glandular fever can produce a similar picture, of course it is possible but it is difficult to give an answer until something is known of the virus of glandular fever. In young children it is sometimes difficult to distinguish rubella from glandular fever either by the eruption, the glandular enlargement, or the changes in the blood, although so far as I know the Paul-Bunnell reaction is invariably negative in rubella. Such evidence as exists is against the identity of glandular fever and lymphocytic meningitis but the possibility has not been fully studied. The distinction from agranulocytic angina may, in rare cases, be difficult on the blood changes alone, since in glandular fever the granulocytes may be severely reduced, even below 1000 per c.mm.

Dr. Fuller considers that his cases benefited by the administration of sulphonamides, but it is possible that recovery would have been equally rapid in their absence. It must be remembered that in glandular fever all the blood-forming tissues are affected including the bone-marrow. If the granulocytes are normal or increased in number probably no harm is done, but I am satisfied that I have seen cases of glandular fever made constitutionally worse by the administration of sulphonamides. As glandular fever invariably subsides without specific treatment there seems little reason for running any risks.

May I point out that the identity of glandular fever and monocytic angina was fully recognised before the discovery of the Paul-Bunnell test? I have seen a certain number of cases of glandular fever since the war began. In the last war, glandular fever was a mere name in an occasional textbook and its existence as an entity was almost universally discredited until the discovery of the mononucleosis in 1920; not a single case was recorded and the only suggestion of its presence was made by Dr. J. Burnford, and attracted no attention.

Portland Place, W.1. H. LETHEBY TIDY.

NON-EFFECT OF PRIMARY ALCOHOLIC EXTRACT OF PITUITARY GLANDS ON DIABETIC PATIENTS

SIR,—In your issue of Dec. 7, 1940, Drs. R. D. Lawrence and F. G. Young have shown that the primary neutral alcohol extract of pituitary glands is not anti-diabetogenic. Likewise Mr. H. P. Marks and Dr. F. G. Young, in the same issue, have shown that this extract does not affect the insulin content of the pancreas of male rats. Through the kindness of Prof. J. C. Meakins and Dr. E. Mason of the Royal Victoria Hospital, and Dr. A. F. Fowler of the Montreal General Hospital, a number of clinical trials in diabetic patients have been made with this extract and the results in all cases have been essentially negative. Dr. R. L. Noble of this department has found no significant change in the insulin content of the pancreas of rats treated with the extract. These results are in complete accord with those reported by Messrs. Lawrence, Young and Marks. It is apparent that the results of preliminary experiments with the primary alcoholic extract of pituitary, which I published at an earlier date, did not justify the conclusion that the extract had a profound effect on carbohydrate metabolism. The publication of the results of such preliminary experiments was a serious error in judgment, to which I now frankly confess.

Department of Biochemistry, McGill University, Montreal, Jan. 3. J. B. COLLIP.

PREVENTION OF DIABETES

SIR,—I am sorry to have given an incorrect impression of Professor Himsworth's views concerning the effect of diet on insulin-sensitivity. Professor Himsworth has clearly stated his belief that insulin-sensitivity is influenced by carbohydrate rather than by other dietary constituents, and in discussing our experiments in which dogs received beef-suet only I should have described the diet as low in carbohydrate, and not as a high-fat regimen. Nevertheless, the significance of the results remains unchanged. In his letter of Feb. 1, Professor Himsworth contradicts an important statement in his communication of Jan. 4. In his first letter he wrote:—

"It is consequently my opinion that the application of the therapeutic measures" (prescription of fasting, high-fat diets and insulin by Haist, Campbell and Best) "recommended by the authors would, instead of resting the damaged pancreas, strain the damaged organ still further, thus tending to accelerate the deterioration of established diabetes."

Professor Himsworth then states in his second letter:—

"I agree with Dr. Young and with Haist, Campbell and Best . . . that the evidence indicates that in *diabetic animals whose disease is not controlled by insulin* the ingestion of excessive amounts of carbohydrate probably exhausts, while restriction of carbohydrate, either by starvation or by giving fat diets, probably rests the remaining insulin-producing tissues."

If this statement had appeared in his first letter it would have established as incorrect his pronouncement that the prescription of fasting and high-fat diets and insulin to patients with established diabetes, by Professor Best and his colleagues, is based not on direct proof but on the authors' interpretation of their experiments; and comment from me would have been unnecessary.

I must not attempt to discuss the complex hypotheses which have emerged from Professor Himsworth's long series of interesting papers, but I would emphasise that his second letter carries the tacit belief that a damaged pancreatic islet differs remarkably from a normal one, in that the former is rested while the latter is strained by a restriction of dietary carbohydrate. This hypothesis is of great interest, but I am not at all clear as to the evidence on which it is based. The experiments of Professor Best and his colleagues (*J. Physiol.* 1940, **97**, 107) in which the feeding of diets of fat or sugar to normal or to long-fasting rats resulted, in all cases, in a subnormal insulin content of the pancreas, apparently cannot be regarded as evidence for or against the usefulness of high-fat or high-carbohydrate diets in the treatment of diabetes, and surely cannot be quoted as evidence for islet damage brought about by restriction of dietary carbohydrate.

Professor Himsworth writes in his second letter :—

"In the *normal* animal . . . large amounts of carbohydrate appear to increase the sensitivity of the animal to insulin so that each unit of insulin becomes more effective and the strain on the pancreas is thus lightened. Similarly restriction of carbohydrate impairs sensitivity to insulin and increases the strain on the pancreas."

Although restriction of carbohydrate impairs insulin sensitivity, why need such a procedure increase the strain on the pancreas? It did not do so in Allen's classical experiments with partially depancreatised dogs, in which the pancreatic remnant was sufficiently "normal" to control the blood-sugar level when dietary carbohydrate was low, but not when it was high. When a diet low in carbohydrate is fed, any diminution in insulin sensitivity can be, and much of the evidence shows that it is, more than compensated for by the reduction in the call on the pancreas to secrete the insulin necessary for the metabolism of carbohydrate. There is no reason to believe that restriction of carbohydrate can cause permanent damage to the insulin-secreting mechanism merely because a sudden increase in dietary glycogenic material may temporarily embarrass the carbohydrate metabolism of an animal whose economy has been adapted to a restriction of exogenous carbohydrate. In my opinion Professor Himsworth has not produced evidence that permanent disuse atrophy of pancreatic islets does occur; and until he has done so it seems reasonable to accept as sound the stimulating suggestions of Professor Best and his colleagues for the prophylactic and therapeutic treatment of diabetes, based as they are on experimental and clinical evidence, both ancient and modern.

National Institute for Medical Research. F. G. YOUNG.

TREATMENT OF WAR NEUROSIS

SIR,—Dr. Dillon raises a number of important issues. An analysis of our case material is being made, and it is hoped that the figures he desires, with many others, will shortly be available. This analysis takes much time and labour, and in the meanwhile only rough approximations can be made. Our material has varied much from time to time. When considerable numbers of acute cases were being treated, it was possible to return up to 60% of them to duty. At the present time, with a more chronic material, the figure is probably nearer 15%. This figure may seem low, but were the discharge rates to duty from base hospitals in the last war any higher? It would be easy to bring our 15% rate up to any desired figure, even 100%, were we concerned more in obtaining superficially brilliant results than in performing our duty to the army and the soldier. This is not therapeutic pessimism, but prognostic caution.

Experience gained in the last war is not easily related to the present one; so many of the circumstances are different. For one thing, home service in the last war was service far from the front, not now. Psychiatry itself has altered much. It is fair to say that it is less superficial than it was; and we certainly know more of the importance of personality and constitutional factors than we did in 1916. While it is true that some excellent soldiers have neurotic qualities, what is prognostically important is the number, kind and severity of these neurotic traits. It is self-evident that no good soldier has neurotic qualities causing any degree of disability. That the average serving sailor, at any rate, has very few neurotic qualities has been clearly shown by the valuable investigation of Drs. Curran and Mallinson. In the good soldier, any existing neurotic traits will be found to be compensated for by positive qualities of personality, determination, tenacity and strength of fibre. Dr. Dillon says that "considerable numbers of men in the last war made good after an attack of war neurosis" even on return to the pathogenic environment. But were there any follow-up statistics? We are now engaged in collecting such statistics, with the aid of administrative arrangements made with the Army, I believe for the first time.

Apart from intensive and prolonged psychotherapy, I do not think there are any important measures of treatment we are leaving untried. We have no lack of "cures"; the number of cases recommended for invaliding whom we do not send back fit for a valuable civilian occupation is very small. To send these men back to the Army would be to replace a fit civilian by a sick soldier, to exchange an asset for a liability. The following two cases illustrate this point, and provide some answer to Dr. Dillon's question, what are our criteria in estimating liability to break down, and what qualitative and quantitative factors we use in assessing the personality. Both were cases that we "cured," but preferred to recommend for invaliding.

1. "Hysteria."—An intelligent man, a surveyor of 35, was admitted with a complete hysterical paralysis below the waist. He could not stand, he could not sit up. He complained of headaches. He was truculent and aggressive. He was "cured" by hypnosis in one session, after which not only the paralysis but also the headaches and the truculence vanished. His father had died in a mental hospital. He had never been a success at his job, being completely without drive or tenacity. He had had three previous attacks of hysterical paraplegia, twice before professional examinations, once after a trivial motor-cycle accident. He was the tortured victim of innumerable obsessional and hysterical tendencies. He had fought well in France up to a point, and had then cracked completely. A week after his cure, his attention was taken up with his obsessional symptoms. A case of conversion hysteria in a psychopath.

2. "Anxiety Neurosis."—A well-built, tall, athletic man of 38, a professional squash-rackets player, was admitted with an effort syndrome. He had broken down under no obvious stress with palpitations, tremblings, dyspnœa on exertion. He was given psychotherapy, graduated exercises and reassurance, and made a complete recovery. Six years ago he had been advised to leave London and professional competition because of his "health]"—i.e., because of certain hypochondriacal preoccupations. He was a reader of "Health and Strength" and had a severe and very prolonged conflict over masturbation. All his life he was never at ease with those of his own social standing, but only happy with superiors and those to whom he could adopt a subservient or dependent attitude. Terrified of fights or disputes, in their vicinity he would become speechless, tremble and palpitate; in all his life, he had never been able to lose his temper. Natural aggressiveness was totally lacking; there was no "fight" in him. He was, in fact, a great husky sensitive plant, a "Ferdinand the Bull."

In these cases it is not the acute neurotic symptoms that are of prognostic importance, but the permanent make-up of the personality. In the first man we see a rigid but fragile and precariously adjusted individual, liable to recurrent breakdown; in the second, a comparatively healthy but feeble personality, without a spark of the aggressiveness that makes a soldier, and permanently incapacitated from coming to terms with his fellows.

Sutton. ELIOT SLATER.

ECONOMICAL USE OF INSULIN

SIR,—In recent months anxious letters from diabetics all over the country, but mostly from small towns and villages, have shown their difficulties in obtaining their accustomed supplies of insulin. Bombs have certainly destroyed some insulin supplies, but not enough to make any real difference to the abundant stocks in this country—of this diabetics and their doctors may rest assured—although local distribution has been temporarily upset. The manufacturers have noted that, besides the annual gradual increase in the sale of insulin, national emergencies (like September, 1939, the fall of France and the

beginning of the air blitz) push up the insulin sales by 20–40% for a few weeks. As a result local supplies are almost depleted, diabetics cannot obtain all they want of their usual make or strength of insulin; they panic a little and press the local chemist who makes unexpected demands on the manufacturer, and so on. A recent article in the *Pharmaceutical Journal* (Dec. 7, 1940) urged chemists to lay in larger stocks of insulin and this, although for the good of diabetics in some ways, had the unfortunate result of putting some manufacturers under difficulties and accentuated the local shortage in some areas. Doctors, chemists and diabetics could help the manufacturers greatly in the adequate distribution of insulin by making no sudden increased calls, but quietly laying in adequate stocks.

By prescribing and using the more *concentrated* strengths of insulin, all concerned could help greatly to contribute to national economy. One of the main difficulties for manufacturers now is the supply of suitable glass for bottles and in this an obvious economy is possible. It is not generally realised that there are three strengths of insulin on the market, 20, 40 and 80 units per c.cm.; by prescribing the stronger solutions large numbers of bottles and packings could be saved. At present the weakest strength is still most widely used and if 40 unit strength insulin were prescribed instead of 20 unit strength, 20,000 bottles a week would be saved. Apart from economy, there are other good reasons for using the stronger insulins. Most patients prefer them, when they know about them, because they reduce the volume of the injection without making the accurate measurement, even with small doses, difficult. Again at present numerous mistakes are made between the three strengths of insulin which would ultimately be reduced by the use of only 2 varieties—40 and 80 unit strengths. This would bring soluble insulin into line with protamine insulin of which no 20 unit strength is manufactured. I have not prescribed the 20 unit strength for four years; I think its disappearance from the market would be a blessing to diabetics and manufacturers. Then we could have a standard insulin solution of 40 unit strength for general use and a stronger solution 80 unit strength for cases on very large doses. To effect such a change I suppose the B.P. Commission and other necessarily slow-moving bodies must be consulted, but in the meantime I would urge the immediate prescription of the stronger insulins by doctors, who should also reassure diabetics, many of whom are ridiculously conservative in their use of one particular make or strength of insulin. Diabetics should be told that all brands and strengths in this country are equally good and active and can replace, if necessary, their favourite bottles, provided the correct adjustment is made in the syringe when the strength is changed. The Americans aptly call and label these insulins, U40 and U80 (clear and short terms) and if this practice was adopted here in bold labels on the bottles dangerous confusion between doctors, nurses and patients would be minimised.

Harley Street, W.1. R. D. LAWRENCE.

*** The Ministry of Health, besides recommending the use of stronger insulin, endorsed by Dr. Lawrence, advise diabetics to carry in their pockets or round their necks or wrists information that they are diabetics taking insulin. The Diabetic Association (124, Baker Street, London, W.1) will supply, on receipt of a stamped envelope, a suitable card on which the usual doses of insulin and the doctor's name and address can be written, and a special identity disc.—ED. L.

POST-WAR HOSPITAL POLICY

SIR,—In your issue of Feb. 1 Sir Farquhar Buzzard sets out four essential requirements for an efficient hospital service:—

1. The voluntary hospitals have failed to provide for the nation's needs, therefore something more is required. "All the changes envisaged in regard to institutional treatment for patients of all classes point to the conclusion that the voluntary hospitals no longer meet the increased medical and health needs of the population."

2. The type of work undertaken by each individual hospital must be determined by some outside regional authority, and hospitals must be developed or suppressed according to the public need. "On the shoulders of these medical advisory committees will fall the responsibility of advising the regional councils in regard to the initiation or development of requisite services or, it may be, the limitation or curtailment of certain services in order to avoid wasteful overlapping or competition."

3. The consultant, as well as the resident staff of hospitals, must reside and work where their services are most needed. Sir Farquhar puts it kindly but firmly in these words: "In some areas it may be advisable for consultants to be nominally on the staff of a key hospital but to reside in an outlying area and serve a group of small hospitals."

4. The consultant staff of a hospital must no longer be expected to trust to the uncertainties of private practice for their remuneration. "The day of the honorary position of hospital staffs has passed and it is necessary to consider the sources from which funds can be found for their stipends."

With all these propositions I entirely agree and I would go further and say that without them an efficient hospital service is impossible. Those of us who believe in national hospitals have expressed these views for years. But does Sir Farquhar really believe that these essentials are going to be achieved by a voluntary self-constituted body like the Nuffield Provisional Hospital Trust? Does he really suppose that a heavily endowed voluntary hospital with strong local support is going to put up with being told what it may and may not do, by a regional council whose only power of control is the provision of monetary grants? Does he suppose that the medical staff who have been in complete control for years are going to agree to a consultant being "dumped" upon them even if some part of his salary is paid by such a regional council? Or, for that matter, is the consultant going to agree to all the unpleasantness of an unwanted post merely for the honour of being nominally on the staff of a key hospital?

In my opinion, for the organisation of the hospitals on a regional basis—so essential at the present time, as I quite agree—some authority greater than a self-constituted trust is required. The authority must be national. It is the people of this country who use the hospitals. It is the people who must control them, through their national and local representatives. It is morally wrong that the quality of service obtainable should have to depend on the success or otherwise of fetes and flag days. An efficient hospital service is a national necessity. It is for the nation to undertake its organisation.

Devonshire Street, W.1. SOMERVILLE HASTINGS.

CONTROL OF THE BED BUG

SIR,—In his paper of Jan. 11 Dr. Busvine says that repeated exposures to the fumes of heavy coal-tar naphtha may cause lesions in the human liver. In case it should be assumed that naphtha is not a safe fumigant, I should like to point out that the experiments to which he referred described certain toxic effects observed on animals exposed to concentrations of coal-tar naphtha vapour far in excess of those to which persons might be exposed during or after a house fumigation. A technique for fumigating empty houses has been described by Ashmore and McKenny Hughes and this process has been in extensive use during the past two years. The danger to occupants of adjoining houses by leakage of vapour is negligible whilst the amount of vapour which might "build up" in a house after fumigation and ventilation, and to which returning occupants might be exposed, can never reach a harmful concentration.

Government Laboratory, W.C.2. S. A. ASHMORE.

THE B.M.A. MEDICAL PLANNING COMMISSION

SIR,—The correspondence which has followed your leading article of Jan. 11 reveals doubts about your claim that the commission may fairly be regarded as representative, while supporting your criticism of the preponderance of elderly members. These doubts may or may not be removed, but if we may judge from past experience of centralised committees it is safe to predict that the main part of the commission's work will be done by a small group who are able to meet regularly. It is also safe to suppose that this group will be composed mainly of London members and of the older provincial members. Time and distance will under war conditions prevent the younger and professionally active members from taking more than a perfunctory part in the proceedings.

We are told that "the visions and aspirations of the younger men and women will not be overlooked." This sounds much more like a condescending gesture than an invitation to coöperation. Indeed it suggests rather that it is the intention of the promoters that the commission shall be dominated by the "less younger" of our colleagues. The fear that the profession will be faced with a fait-accompli has already been expressed. But even this is perhaps not the greatest danger. Surely the most serious result of an unrepresentative report is the deep division within the profession which it is likely to produce. The spectacle of a divided profession is not one to dispose Parliament to give that consideration to medical opinion which is desirable.

Better no report than a disputed report. Is this now inevitable? One can but hope that it is not. Is it too late to urge the reorganisation of the commission on a regional basis? It is widely believed that a regional medical service has the best prospect of success, and in any event regional problems and conditions must be given full and knowledgeable consideration. Adequate representation, backed by the regular attendance of members, would be ensured and an agreed report could be expected. The suggestion is that 7 or 8 regional committees, preferably elected, would be set up, together with several special committees to deal with specific problems. These committees would work simultaneously according to an agreed programme, and would report at regular intervals to a central body, which would be composed of representatives of the committees together with an equal number of members nominated by such bodies as the royal colleges, the medical schools, and the B.M.A. The chairman could profitably be a wise and judicial layman!

The function of this central body would be the progressive integration of the committee reports into a balanced whole. The widest publicity in the medical press throughout the proceedings is an essential feature. It is considered that the less frequent meetings of this much smaller body need present no obstacle to regular attendance, especially if the provincial members were compensated for their time and their expenses defrayed —as indeed is only fair. It is true that the B.M.A. has promised that divisions and branches "will have a chance to study and if necessary to criticise" the findings of the commission. But if this is to be considered as a method of discovering and focusing the considered view of the profession on the vast problems under discussion, it is surely a reductio ad absurdum in excelsis. What division or branch, faced with a document of 300 or 400 pages, could adequately digest, let alone criticise, it within a reasonable time. And if they could, what effect are their several and possibly diverse critiques likely to produce? We all know the answer. Furthermore, not all the members of the profession are members of the B.M.A. or other bodies "represented" in the commission as at present constituted.

We have a chance to mould a future national medical service. Let us not lose it.

Newcastle-upon-Tyne. A. G. OGILVIE.

SIR,—There must be many in the medical profession who would agree with the doctors of Newcastle-upon-Tyne in thinking that the reorganisation of the medical profession must affect the general public, and that Parliament is the proper body to express the policy of the people. The experience we are now reaping of bureaucratic control in medicine is not, I think, likely to yield a harvest of totalitarians. There is a vast difference between the conception of the schools as to what medicine should be and what it really is, as met with in the homes of the people. Speaking for the general practitioner Osler said "Our study is man. Were he always, inside and out, cast in the same mould, instead of differing from his fellow man as much in constitution and in his reaction to stimulus as in feature, we should, ere this, have reached some settled principles in our art." Totalitarianism ignores the individual and bases its action on principles settled by a self-appointed dictatorship, which, as it seems in the case of the Medical Planning Commission, is to be vested in a body of men, drawn largely from the schools, who have little idea of the conditions that pertain at the point where medical practice and the general public meet.

The subtle relationship between patient and doctor defies definition, and an attempt by the state to define it must, surely, be disastrous for both patient and doctor. For the patient it would mean, at the least, the loss of a very particular friend, and for the doctor, to quote Osler again, "the peril is that should he cease to think for himself he would become a mere automaton." We have yet to find perfection along democratic paths; democracy has not yet had a fair trial, but we are now at the parting of the ways, and there are only two ways—to democracy and to totalitarianism. Which is it to be?

Torquay. PAUL C. GIBSON.

CARBON-DIOXIDE TREATMENT OF WOUNDS

SIR,—In 1770 M. Percival, a friend of Priestley, applied with success "fixed air" (carbon dioxide) to badly healing wounds. Much later a French surgeon, Demarquai, described in 1859 and 1862 how ulcers and gangrene which had resisted other treatment healed under carbon-dioxide treatment with remarkable rapidity. These observations were lost sight of until A. Benatt (1933) published details of five cases of cyanotic ulcers which were treated first with local warm water baths, then with saline baths, and finally with saline and carbon-dioxide baths; the effects on the capillary blood-flow being observed in each case microscopically. While saline baths improved the ulcers the addition of carbon dioxide healed them quickly. The skin up to the level of the bath showed marked hyperæmia to the naked eye, rapid capillary blood-flow being now observable on microscopic examination, and the appearance of capillaries which were before invisible. Carbon-dioxide baths have since been used with success in Germany for the treatment of diabetic gangrene, decubitus, third-degree burns and wounds. Combining salt and carbon-dioxide baths at the St. John Clinic Benatt has found Dead Sea salt in concentration of 5–6% to be not irritating (while solutions of common salt may be painful, as is the combination of many salt compounds present in natural springs). After the wounded limb is enclosed in plaster carbon-dioxide treatment can be applied, for the gas penetrates even thick layers of dressings. The gas should be moistened by passing it through water. A feeling of warmth indicates when the gas begins to produce hyperæmia of the skin.

St. John Clinic, S.W.1. LEONARD HILL.

PLIGHT OF THE SERVING PRACTITIONER

SIR,—Sir Ernest Graham-Little's letter to the *Times* on medical practice encourages me to write about the very serious position of young practitioners who have left their practices to serve. I will cite an example. A well-qualified doctor with a family bought a practice before the war at a cost of about £4000. Not having much capital he raised most of the sum by a loan from an insurance company on the security of the practice and a ten-year endowment policy to the amount borrowed. As a medical officer on the volunteer reserve of one of the fighting services he left the practice at a moment's notice at the outbreak of war, and his income became about £430 a year, plus marriage allowances of about £140 and a small income through the Protection of Practices Bureau. On this he was expected to pay interest and premiums for many future years for the purchase of a practice which owing to the war had disappeared. The only relief offered him is postponement of his repayments, which is really slavery under the euphemism of "moratorium." There is urgent need for legislation to compensate him for his loss—more urgent than for many losses to property which the War Damage Bill will cover.

Could not the insurance companies, who protect themselves from loss by charging him 5% of the sum loaned as a "guarantee premium" so that they may insure themselves against loss, rightly take up their guarantee under the circumstances of complete or almost complete loss due to war, so that the doctor would not be left with the choice of the stigma of bankruptcy or slavery and inability to meet his family obligations? Could not the representatives of the profession secure relief for him as it is being secured for property-owners who have made no such great sacrifice? I should be grateful to hear what your readers think of the ethical aspect of the matter. Are the rich insurance companies to be artificially protected from the losses due to war by leaving the whole of the loss to be borne by the doctor? M.D.

SULPHATHIAZOLE IN CEREBROSPINAL FEVER

SIR,—Dr. Banks must be complimented on his results in the treatment of cerebrospinal fever with sulphathiazole. Since the introduction of chemotherapy the results have undoubtedly been much better than when serum was used, but the claims put forward that the death-rate has been reduced to the low figure of 2–10% by chemotherapy are not supported by the official returns. The Registrar-General's weekly returns for London show that during 1940 there were 868 cases of cerebrospinal fever notified, with 158 deaths (fatality 18%), and for Sheffield 235 notifications, with 46 deaths (fatality 19·6%). During the year 1940, 235 Sheffield cases and 79 cases from the Chesterfield area were treated at this hospital, with 70 deaths (22%). Of these 70 deaths, 35 occurred within 24 hours of admission to hospital. Every case was treated with sulphapyridine in dosage even higher than that suggested by Dr. Banks. All patients suffering from the malady in Sheffield and district were admitted direct to this hospital, whereas in Dr. Banks's paper he thanks other London hospitals for the transfer of the cases. I assume that only patients fit to be removed would be transferred to the Park Hospital. I feel sure a similar type of fulminating case dying within 12–36 hours of the onset of the disease occurred in London, as in Sheffield, and did not come to Dr. Banks. It would be helpful to know the number of cases transferred to the Park Hospital, and if possible the number of deaths that took place at the other London hospitals before transfer could be carried out. Or perhaps an explanation of the London returns showing 868 notifications and 158 deaths could be offered?

Lodge Moor Hospital, Sheffield. J. M. KENNEDY.

PAPWORTH INDUSTRIES

SIR,—As one who from childhood has had the privilege of knowing the late Sir Pendrill Varrier-Jones, and who for the last six years has enjoyed not only his close friendship but also his personal guidance in the operation of the principles upon which his work is founded, I should like to write a few words about the Papworth Industries. Instituted during the Four Years War they began on a small scale; and they grew as more and more patients from the hospitals decided, after treatment, to throw in their lot with Papworth and to participate in what was at first a pioneer experiment. Because Sir Pendrill built each department around a personality, and insisted that the patients and ex-patients should have the aid of modern machines; because, too, he encouraged the workers to accept responsibility and gave them every opportunity of advancement, the industries grew and prospered and their scope increased. Now in their several main departments—carpentry, cabinet-making, leather goods, printing, upholstery and building—they give employment to hundreds of former patients at rates of pay fixed in agreement with the trade-unions.

In the application of Papworth's principles, and in the axiom "machinery compensates disability" first enunciated by Sir Pendrill, the economic problems of many of the disabled have been solved; and we believe that by following closely the way he charted so thoroughly for us his work will live and develop as he would have wished.

PETER FRASER,
Managing Director of Papworth and Enham Industries.

FIRST-AID FOR THE SOLDIER

SIR,—Soldiers expect to take risks, but some of the men with whom I served in France need not have died and many more are today minus limbs who might still be whole. One of the important lessons we learned in France was the prevention, as far as possible, of serious casualties. A wounded soldier is a liability to himself and everyone else, and practical first-aid should be included in a recruit's syllabus. A soldier is taught how to kill and destroy, how to operate and fire his weapons, and the best way to protect himself against similar weapons, but not one lesson does he receive on how to save his comrade's life.

The reason for this, I feel sure, is that the Army control is too stereotyped and orthodox. The Army books say that the enemy's front shall be opposite our own, and at the rear of our front we shall have a regimental aid-post and behind that a properly equipped hospital. Therefore the Army is satisfied that all wounded will receive prompt and efficient treatment. Yet the object-lesson of our all too brief sojourn in France was that in modern war there is no such thing as a "front." Mechanised forces move too quickly for that, so there are bound to be small numbers of men isolated from the main body. One has only to read of the retreat of the Italian army before the Greeks to realise that. Therefore I strongly maintain that every soldier should know how to set broken limbs, stop arterial bleeding and should have a really sound knowledge of first-aid. I do not say that a soldier should be equipped with a scalpel and a bottle of chloroform, but he must be taught how to help a wounded comrade. More important still, he must know what not to do. As our medical officer said in reply to a question of mine, "Bad first-aid is often worse than no first-aid." My answer to that is "Every soldier must know how to apply good first-aid."

One would have thought that the terrible butchery that took place during the last war would have driven home the point, for thousands of men died because of their comrades' ignorance. That must not happen during this war. It is not too late, for although the average M.O. is a very busy man he would be only too pleased to give lectures. Think how much simpler his job would be if wounded men received the right kind of first-aid before they were sent to him. The importance of this subject cannot be overstressed, and I shall feel happier and safer when I see practical first-aid included in a soldier's training programme.

LANCE-CORPORAL.

CHILLY SWEEPER

SIR,—If Adam Levite had the most elementary idea of sociology he would realise that publicity, not charity, rectifies intolerable social conditions. It is a mighty shout, not an odd half-crown, which brings down the walls of Jericho where the Levites live.

Harley Street, W.1. CLIFFORD ALLEN.

Obituary

WILLIAM ARTHUR REES

O.B.E., M.D. LOND., F.R.C.S.

Dr. W. A. Rees, who died on Jan. 29, was born in India in 1878, the son of the late F. W. J. Rees, B.C.A. He was educated at Haileybury College and the Middlesex Hospital. He qualified in 1902 and took his M.B. Lond. the following year. To fit himself for practice, he spent several years in resident appointments and post-graduate study, obtaining the F.R.C.S. in 1904 and his M.D. two years later. Finally he set up in practice at Swanage where he died.

One of his teachers, who has a keen recollection of his ability, industry and readiness to help, writes:—

The death of Dr. W. A. Rees will cause sorrow to all who have known him from his student days and appreciated his sterling qualities. He had an attractive though very modest personality, so that it may be questioned if he ever realised how great were his professional gifts and attainments, for he was never a man to air his opinions or to seek recognition. He was universally popular and universally trusted, remarkably so for a man who was in some degree shy and retiring.

ANDREW SPROTT

M.B. GLASG.

Dr. Andrew Sprott, who died in Appleby on Jan. 29 at the age of 74, was born in Wigtownshire and educated at Glasgow University where he graduated in 1887. After serving as an assistant to the late Dr. J. W. Fawcitt, of Broughton-in-Furness, whose sister he married, he spent some years in practice at Glenridding on the shores of Lake Ullswater. He then moved to Appleby, where he built up a large practice from which he retired only three years ago. During the last war he was medical officer to the Appleby Red Cross Hospital, and later became the county director of the British Red Cross Association. He was a service brother of the Venerable Order of the Hospital of St. John of Jerusalem. He is survived by his widow, one of three sons, and a daughter.

Mr. J. N. J. Hartley writes: "Dr. Andrew Sprott will long be affectionately remembered in Appleby and the

surrounding district where he spent most of his active years. He was a keen fisher, and a great student of nature. Perhaps his chief hobby was field botany, in which he was recognised as an authority. His colleagues and friends will treasure memories of his good fellowship and his stimulating personality, and will regret that he was not spared longer to enjoy his garden and the countryside of which he was so fond."

GEORGE DANSEY-BROWNING

C.B.E., M.R.C.P., D.P.H., D.T.M.
COLONEL, LATE R.A.M.C.

Colonel George Dansey-Browning, who died on Feb. 2, during his years of service and during his so-called retirement worked hard for the welfare of the soldier and his family. Born in 1870, he was educated at the Royal Naval School, and at the Lorient Lycée in Rennes where he acquired his easy mastery of the French language. He qualified from the Westminster Hospital in 1897 and passed by competition into the Army Medical School at Netley. Before he sailed for China in 1900 he had already taken his D.P.H. and on subsequent leaves at home he added to his qualifications the D.T.M. and the M.R.C.P. For his work in China he was awarded the China medal in 1900. Later he was appointed medical officer of health for Gibraltar, and he held this responsible post during the last war. For his services at the busy port he was awarded the C.B.E. in 1919 and the French medal for epidemics. In 1922 he was appointed assistant director of medical services for the U.P. district of India with his headquarters at Lucknow. On his retirement he was appointed medical director of Enham Village Centre for disabled ex-Service men which was then being started. When his work of organisation was accomplished there he had equal scope as medical officer to the troops at Longmoor where his care for the soldiers' wives and children was unflagging.

He married in 1907 Lilian Stoddart and they had a daughter and a son, Major Charles Dansey-Browning, who is serving with the R.A.M.C.

JAMES BELL

M.D., SC.D. DUBL., F.C.S.

Dr. James Bell, fellow of Trinity College, who died recently, aged 42, after an illness of seven months, was born in Belfast and educated there at the Royal Academical Institution. He entered Trinity College in 1916, and graduated in 1920 with honours in mathematics and experimental science. He continued his study of physiology and in 1927 was appointed lecturer in biophysics in the School of Physics in Trinity College. While holding that post he studied medicine and in 1934 graduated M.B. and in the following year he was elected a fellow of the college. Although he was a lucid and painstaking teacher and a man of science of considerable originality it was by his discharge of his duties as college tutor that he made his mark on the men of his time in the university. He was in truth the college guardian of his pupils, watching over their careers, and guiding and advising them. In his younger days he played Rugby for the university and while a fellow of the college he became an officer in the volunteer corps under the government of the Irish Free State. He was the first volunteer officer to receive a commission in the regular forces of Eire. He was called up when the war began and he was actually serving when his illness first showed itself last summer, though later he was seconded to return to his college duties. Trinity College has lost a member of its staff who was loved and respected by his colleagues and by his students.

WINIFRED PORTER

M.B. MANC.

Dr. Winifred Porter, who was killed during an air-raid on the night of Jan. 29, graduated from the University of Manchester in 1934. After holding house-appointments at the South London Hospital for Women and the Victoria Hospital for Children in Tite Street, she went as a temporary assistant physician to the Retreat, York. When she died she was serving at an L.C.C. mental hospital. A colleague writes: Dr. Porter was a woman of intelligence and charm. In her work she was efficient and as an anæsthetist she was outstanding. She had a sharp clinical acumen and went straight to the core of any matter in hand. She had the good of her patients at heart, and took a keen interest in the welfare of the nursing staff in her wards. She loved the truth and was fearless in the expression of her opinions when she felt them justified.

She was engaged to Surgeon Lieutenant K. J. O'Connor, R.N.

Medical News

University of Cambridge

On Feb. 7 the following degrees were conferred:—

M.D.—*O. N. Roussel.
M.B., B.Chir.—*W. B. D. Maile, *H. D. S. Vellacott, by E. H. Enderby and D. N. White.

*By proxy.

The title of the degrees of M.B., B.Chir. has been conferred on P. G. Holman.

The Society of Medical Officers of Health are entertaining Surgeon-General Thomas Parran of the United States public-health service at luncheon on Friday, Feb. 21, at the Piccadilly Hotel, W.1 at 1 P.M. Members of the society may obtain tickets at 7*s.* 6*d.* each from the acting executive secretary at Tavistock House South, Tavistock Square, W.C.1, not later than Feb. 19. They may be accompanied by one representative of their local authority.

The next meeting of the Shaftesbury Military Hospital Medical Society will be held on Tuesday, Feb. 18, at the hospital, when Colonel L. E. H. Whitby will speak on transfusion for war conditions. Beginning on Feb. 19 there will be a teaching round in the medical division of the hospital at 2.30 P.M. each Wednesday, and in the surgical division at 2.30 P.M. on alternate Tuesdays beginning on Feb. 25.

The therapy section of the Faculty of Radiologists will meet at 32, Welbeck Street, London, W.1, on Friday, Feb. 21, at 10.30 A.M., when Mr. Malcolm Donaldson will open a discussion on the organisation of radiotherapy in war-time. Mr. E. Rock Carling, Mr. G. F. Stebbing and Dr. Ralston Paterson will also speak. At 2 P.M. Dr. Paterson will deliver the Skinner lecture to the faculty. His subject will be cancer of the bladder. At 3 P.M., Dr. Stefan Engel will demonstrate the anatomy and radiology of the bronchial glands to the diagnostic section.

The Medical Women's Federation is arranging for a course of six lectures on social anthropology to be given at the London School of Hygiene from March 3 to 8 at 4.30 P.M. The course is intended for doctors and nurses working overseas, but members of the public interested will be welcome. The lecturers will be Miss Margaret Read, Ph.D., acting head of the colonial department of the Institute of Education, University of London, and Miss M. M. Green, lecturer at the School of Oriental and African Studies. Tickets for the course and further information may be had from Dr. Margaret Balfour, 14, Sylvan Road, Upper Norwood, London, S.E.19, or at the first lecture.

The executive committee of the Socialist Medical Association have passed a resolution stating that they consider that the imposition of a Purchase Tax on non-proprietary drugs and medicines is detrimental to the health and well-being of the nation. They call upon the Government to abolish the Purchase Tax on the following items, provided that no trade name or proprietary right is claimed in connexion with them:—

(*a*) all preparations of the British Pharmacopœia and British Pharmaceutical Codex,
(*b*) all other drugs and medicines if supplied on the prescription of a qualified practitioner.

The Minister of Health has informed local food committees that in future diabetics are to receive a triple meat ration. Up till now they have been receiving double the ordinary ration. Diabetic patients may obtain from the Diabetic Association (124, Baker Street, W.1) a card on which to write their usual dose of insulin, the treatment for an overdose and their doctor's name and address. The Minister urges that the diabetic should always carry this information on his person.

The personnel of the War Emergency Formulary Committee appointed by the Ministry of Health is as follows:—

Mr. H. Davis, Ph.D. (representing the voluntary hospitals); Dr. E. A. Gregg (British Medical Association); Prof. J. A. Gunn, D.M. (Pharmacopœia Commission); Dr. Philip Hamill (Royal College of Physicians); Dr. C. H. Hampshire (Therapeutic Requirements Committee of the Medical Research Council); Mr. R. Dawson Hutchinson (Ministry of Health); Dr. Lewis Lilley (British Medical

Association); Mr. H. N. Linstead, Ph. C. (Pharmaceutical Society); Mr. A. R. Melhuish, Ph.C. (National Pharmaceutical Union); Mr. A. Mortimer (Wholesale Drug Trade Association); Mr. F. B. Royal (London County Council); and Dr. J. W. G. Steell (Ministry of Health.)

The secretary of the committee is Mr. H. L. F. Walton, who may be addressed at room 559 of the ministry, Caxton House West, Tothill Street, Westminster, London, S.W.1.

A George medal has been awarded to Dr. Malcolm Manson, medical officer of health for Wood Green.

A recent casualty list confirms that T/Major P. H. Newman, F.R.C.S., who was previously reported missing believed prisoner of war, is now a prisoner of war.

Vacancies for examining surgeons under the Factories Act 1937 are announced in our advertisement columns. In the circumstances of the times these appointments are of growing interest and importance. Particulars may be had from the chief inspector of factories, Cleland House, Page Street, London, S.W.1.

The Local Authorities' Nursing Services Joint Committee, which is the nursing section of the National Joint Council for Local Authorities' Administrative, Technical and Clerical Services has lately held its first meeting, under the chairmanship of Councillor W. J. P. Webber. It has been set up to consider, both nationally and regionally, the salaries and conditions of work of employees in the nursing services of county councils, county and non-county boroughs, urban and rural district councils and joint boards. Of the 16 seats accorded to the staffs side on the joint committee, 8 are filled by members of the Royal College of Nursing. The other 8 places are allotted to other associations granting membership to nurses—namely, the National Association of Local Government Officers, National Union of Public Employees, and Transport and General Workers' Union. The college, however, is the only body so far whose representatives are actually practising nurses.

Births, Marriages and Deaths

BIRTHS

BRYSON.—On Feb. 5, at Beaconsfield, the wife of Dr. Charles C. Bryson—a daughter.

COULTHARD.—On Feb. 1, at Esher, the wife of Mr. J. Jefferson Coulthard, F.R.C.S.E.—a daughter.

FREW.—On Jan. 23, in New York, the wife of Dr. John Frew, of Stafford—a daughter.

GARDINER.—On Feb. 4, in Leeds, the wife of Dr. Malcolm Gardiner—a daughter.

HAINES.—On Feb. 6, at Oxford, the wife of Dr. Magnus Haines—a daughter.

MCINTOSH.—On Jan. 31, at Leaverstock Green, the wife of Dr. J. M. D. McIntosh—a daughter.

MCSWINEY.—On Jan. 27, at Godalming, the wife of Prof. B. A. McSwiney—a son.

ORCHARD.—On Feb. 4, at Truro, the wife of Dr. Stuart Orchard—a son.

SANDEMAN.—On Feb. 5, the wife of Temp. Surgeon Lieutenant C. Stewart Sandeman, M.B., R.N.V.R.—a son.

WATSON.—On Feb. 4, at Southborough, Kent, the wife of Lieutenant Martin B. Watson, M.R.C.S., R.A.M.C.—a son.

YOUNG.—On Feb. 8, at Basingstoke, the wife of Dr. C. A. Young—a son.

MARRIAGES

M'KELVIE—COWIE.—On Jan. 1, at Khartoum, Alexander Robertson M'Kelvie, M.B., Sudan Medical Service, to Jessie Bryden.

VELLACOTT—TIBBS.—On Feb. 10, at Plymouth, Hugh Douglas Sempill Vellacott, M.B., son of Mr. H. F. Vellacott, F.R.C.S., to Lorraine Freda Tibbs.

DEATHS

ALLAN.—On Jan. 28, at Roundhay, Leeds, in his 88th year, James Allan, M.D. Aberd., D.P.H. Camb., late medical superintendent, St. James's Hospital, Leeds.

BANKS.—On Feb. 7, at Aberdare, Isaac Banks, O.B.E., M.D. R.U.I., J.P., aged 73.

COSENS.—On Feb. 10, at Worthing, William Burrough Cosens, M.R.C.S., aged 79.

FRYER.—On Feb. 8, at Shanklin, Charles Fryer, L.R.C.P.E., aged 86.

KIRKPATRICK.—On Feb. 8, at Sherborne, Dorset, William Kirkpatrick, M.D. Dubl., aged 79.

PENFOLD.—On Jan. 31, Fred Bailey Penfold, M.R.C.S., of Leatherhead, aged 62.

PRIESTLEY.—On Feb. 9, at March Baldon, John Gillies Priestley, M.C., D.M. Oxfd, reader and demonstrator in clinical physiology in the University of Oxford, aged 61.

SAUNDER.—On Jan. 31, at Barnes, Charles Stirling Saunder, L.R.C.P., aged 81.

SCURFIELD.—On Feb. 8, at Letchworth, Harold Scurfield, M.D. Edin., D.P.H.

SHARP.—On Jan. 29, at Corfe, Taunton, John Sharp, M.B. Glasg.

SHEARER.—On Feb. 7, at Cambridge, Cresswell Shearer, M.D. McGill, D.Sc. Camb., F.R.S., formerly lecturer in embryology in the University of Cambridge.

STOTT.—On Feb. 5, at Aberdeen, William Gordon Stott, M.B. Aberd., fleet surgeon, R.N. (retd.).

WOOD.—On Feb. 10, at Penshurst, Louis Edmund Wood, M.B. Lond., aged 83.

Notes, Comments and Abstracts

OCCUPATIONAL DISORDERS IN THE EIGHTEENTH CENTURY

THE first book on occupational diseases—De Morbis Artificum, by Bernardini Ramazzini—was first published in 1700 and a revised edition was issued in 1713 with 12 new chapters and alterations in the original text. A new translation (Diseases of Workers. London: Cambridge University Press. 30s.), prepared by Professor Wilmer Cave Wright, comes like a beaker full of the warm South. The edition of 1700 was translated into English in 1705 by an anonymous writer whose version, as Professor Wright points out, was vigorous and scholarly but far from literal and in many pages he had omitted phrases or sentences. In 1746 Dr. Robert James translated the extra 12 chapters and added them to the anonymous English version of 1705 without indicating that the latter was not his own. Professor Wright in this instance has translated Ramazzini's final edition of 1713 which becomes available in English for the first time and which has been made as literal as possible and is given without omissions. The Latin text accompanies the English rendering on corresponding pages after the fashion of the "cribs" on which our Latin masters frowned so fiercely, so that the reader has to repress a vestigial sense of guilt at seeing the Latin and English in, as it were, an unholy alliance. The translation itself does not read like one because it is in clear flexible English with a fine feeling for the right word. Professor Wright introduces her text with a neat account of Ramazzini's life, achievements and social background, although she modestly avers that it is little more than a bibliography. Yet she succeeds in painting a portrait of an eminently cultured and sympathetic man of great energy, wide interests and outstanding intellectual honesty. The major part of his life's work and literary output was concerned with meteorology and epidemiology, but his fame rests on his studies of occupational diseases—to him almost a sideline. His sympathy for the working classes took him into factories to see actual working conditions for himself and to consider what could be done to alleviate them and prevent ill health. In his preface Ramazzini says that every doctor at his first visit to a patient should ask what occupation he follows. It appears that in his day practitioners were surprisingly negligent about this precaution but Professor Wright generously comments that as a layman she can only assume that such an omission could not occur today. This elegant book is one of the History of Medicine Series issued under the auspices of the library of the New York Academy of Medicine, and it will delight the bibliophile as well as those whose special interests include the history of medicine or occupational diseases.

MASKS FOR SHELTERERS

THE masks promised by the Ministry of Health are to be issued to people using the public shelters if an influenza or other epidemic arises. The standard type is to be a piece of non-inflammable film, 5½ in. square, which is fastened so as to screen the nose and mouth by means of an elastic band passing round the head. Directions for making substitutes have been drawn up, and these can be followed by anyone capable of using a needle and thread. Substitutes can be made from Cellophane, oiled silk or paper; or surgeons masks—pads of muslin or gauze, fastening behind the head with tapes—can be used. A yashmak type of mask can easily be made from a piece of lawn or ninon, 12 in. by 18 in., with a triangle of oiled silk stitched in, to cover the nose and mouth area. The upper border is slightly gathered by two rows of elastic thread and tapes sewn at the corners are tied behind the head. If the maker lacks a piece of oiled silk he can make the reinforced area as a pocket into which a triangle of cellophane can be slipped; or it can be made impervious by painting with a layer of transparent or coloured lacquer which can be bought from ironmongers. Wearers are directed to wash their masks after use. The Ministry has arranged for 500,000 of the standard film masks to be supplied to public shelters.

RESPIRATORS FOR SPECIAL CASES

SOME of us are gas-mask faced and take kindly to our black and green pig-snouts. Others are more casually designed, with oddly shaped heads or jaws; some breathe with difficulty at the best of times and some have the bad luck to wear tracheotomy tubes. The Ministry of Home Security has announced that two new devices are ready to protect those who cannot wear the civilian gas mask. People with severe respiratory difficulties—due to asthma, phthisis, old empyema or cardiac disease—find difficulty in expiring forcibly enough to overcome the resistance of the ordinary mask, but they may be able to manage with the new mask provided with an outlet valve. Severe cases will need the new helmet type of respirator which consists of a hood of rubberised fabric fitting the shoulders and stiffened so that it retains its shape; it is provided with non-inflammable eye pieces and an air-supply unit, similar to that of the baby's helmet, by which the wearer pumps air into the interior. The hood is attached below to a loose skirt which is held in position by strings fastening under the armpits; this stabilises the whole helmet. The air-supply unit juts out and downwards like a snout below the eye-holes; it consists of a pipe containing a standard respirator container and connected to a bellows. The hood is so large that the wearer can stop pumping for a few minutes without ill effect. Air leaves the hood round the bottom edge through the fabric of the porous skirt. This respirator has been designed by Government research workers and is adapted for wear by those with tracheotomy openings. Other devices such as that suggested by Mr. A. Radcliffe[1] for the use of such patients have depended on fitting a gas-tight pad over the tracheotomy opening; but the Government investigators found that only a small proportion of patients could be fitted successfully in this way because in many the neck was thin and shrunken or the opening deeply recessed. Moreover the tube might need frequent clearance. The entry for air in the helmet respirator is directly opposite the tracheotomy opening, which is found to make for comfort; and the wearer can slip a hand inside the hood to clear the tube if it gets blocked. Others likely to benefit from these respirators are those with large or distorted heads, such as acromegalics, patients with tumours of the face or neck, or distorting scars such as those produced by removal of part of the jaw, or tender scars from war injury. The helmets will only be given to those who produce a doctor's certificate showing that such provision is necessary, and medical officers of health have been advised to get into touch with doctors in their area and to decide on a common policy on giving certificates.

The Coventry and Warwickshire Hospital was evacuated after the heavy raid on the city in November. Since then the hospital has been unable to secure suitable accommodation outside the city and as they consider it essential that hospital services should be available they have decided to reopen 230 beds at the hospital including 50 at Keresley.

1. *Lancet*, 1940, **2**, 393.

ANOTHER SCALE OF FAMILY COEFFICIENTS

F. W. Clements (*J. Hyg., Camb.* 1940, **40**, 681) has attempted to determine statistically a scale of family coefficients based on the calories purchased by families surveyed by the advisory council on nutrition of the Commonwealth of Australia. The scale adopted agrees more closely with that of Lusk than with any other. It is:—

Adult man (3013 net calories)	1·0	Child—	
Woman	0·8	6–7	0·62
Child—		4–5	0·61
12–15	0·76	2–3	0·51
10–11	0·72	Under 2	0·47
8–9	0·65		

It is difficult to understand why we must add another to the dozens of proposed scales of family coefficients. It is rather like learning to write verse in the hypothetical language of Erewhon. Even if there were any fixed and firm coefficient for any individual for calories it would not be the same for the other components of diet. There is one coefficient (if one at all) for calories, and another for protein, another for calcium and another for iron, and so on through the gamut of the multitudinous vitamins. In the search for coefficients there is a darkening of nutritional counsel.

NAMES FOR VACCINES

CONFUSION has arisen over the exact meaning of "T.A.B.C. vaccine." Some people use it for the vaccine containing the three strains of paratyphoid, and others for the vaccine containing two strains of paratyphoid plus cholera vaccine. The Minister of Health has approved the following "proper names" for these two Dromios:

1. Anti-typhoid-paratyphoid A, B and C vaccine.
2. Anti-typhoid paratyphoid A and B and cholera vaccine.

He directs that the latter name should not be abbreviated. It should be easy enough to enforce this when the name appears in print or writing—containers are to be relabelled as soon as the present stock of labels is exhausted—but the tongue is lazier than the pen. Those who are so colloquially-minded that they recall improper names more readily than proper ones had better accustom themselves to thinking in terms of "T.A.B.C." and "T.A.B.Chol."

MESSRS. EVANS SONS LESCHER AND WEBB have introduced their Streptocide Bacteriostatic Insufflator for the local treatment of wounds with sulphanilamide. The insufflator was designed in collaboration with Colonel Leonard Colebrook and is based on Legroux's model which he described in our columns (*Lancet*, 1940, **2**, 113). With it a fine mist of streptocide powder can be evenly distributed throughout the wounded tissues.

DIPHENAN B.D.H. is *p*-benzylphenyl carbamate and British Drug Houses (London) are issuing it in tablets of 0·5 gramme for use as an anthelminthic in threadworm infestation. It is claimed that diphenan not only effects the expulsion of the worms from the host but is also a powerful vermicide. It is almost tasteless and is given three times daily by mouth for a seven-day course. No toxic effects have been reported.

LANCET CROSSWORD.—Missing clue from last week's crossword. 17 down. With knobs on. The solution will appear next week.

Brigadier J. A. Manifold has been appointed deputy director of medical services in the Scottish Command, with the rank of major-general. Brigadier D. T. Richardson will succeed him in his present appointment as director of hygiene at the War Office. Brigadier O. W. McSheehy has been appointed deputy director of medical services in the eastern command, and Brigadier Alexander Hood will succeed him as deputy director-general of Army Medical Services at the War Office.

Appointments

CRAWFORD, D. K., M.B. Edin., F.R.C.S.E.: examining surgeon under the Factories Act 1937 for Berkhamsted, Herts.

GRAY, J. DUNCAN, M.B. Sheff.: R.S.O. at Sheffield Royal Hospital.

O'DONNELL, M. J., M.B. N.U.I.: temp. asst. county M.O. for the Isle of Ely.

PEARCE, A. H. B., L.R.C.P.E., D.P.H.: deputy D.M.S. for British Guiana.

SEWELL, ADA M., M.B. Edin.: asst. M.O.H. for Kent.